

MEDICAL INNOVATION IN THE CHANGING HEALTHCARE MARKETPLACE

CONFERENCE SUMMARY

Philip Aspden, Editor

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Policy and Global Affairs
Board on Health Care Services
Institute of Medicine

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Preface

Throughout the 1990s the U.S. health care system underwent significant changes. There were concerted efforts by large corporations and government purchasers of health care to limit increases in health care costs. In particular, managed care organizations sought to introduce greater selectivity in providing services. At the same time, the Clinton Administration committed to doubling the NIH research budget over 10 years. The Bush Administration subsequently endorsed this commitment. Throughout the decade pharmaceutical companies significantly increased their investment in R&D, and Congress instigated a fee-based system at the FDA to accelerate the review and approval of new drugs. There were also important changes on the demand side. The largest consumers of health care, the population over 65 years, increased at a much faster rate than the overall population. Health care consumers, particularly “baby boomers”, became better informed, increasingly through information drawn from the world-wide web, and, as a consequence, more demanding.

Against the background of a wave of new health care innovation and a growing demand for health care coupled with continuing concerns about escalating health care costs, the National Academies’ Board on Science, Technology, and Economic Policy (STEP) and the Board on Health Care Services initiated a project to identify the public policies needed to stimulate the development, adoption, and diffusion of high-value medical innovation. As a first step a conference on “Medical Innovation in the Changing Healthcare Marketplace” was convened June 14–15, 2001 in Washington, D.C.

For the STEP Board, concern with medical technology is part of an ongoing examination of economic performance and innovation changes at the sectoral level. In 1999, the Board completed *U.S. Industry in 2000: Studies in Competitive Performance*,¹ a study of the competitive performance in eleven industries, including the pharmaceuticals industry. For the Board on Health Care Services, the project builds on important parts of two reports of the Committee on the Quality of Health Care in America—*To Err Is Human: Building a Safer Health System*² and *Crossing the Quality Chasm: A New Health System for the 21st Century*.³ The project also seeks to update earlier work of the Board on Health Care Services and the former Council on Health Care Technology. Between 1989 and 1993, an IOM committee on technological innovation in medicine convened five workshops to “critically examine the process by which biomedical research is translated into actual benefits in medical practice.” Proceedings of each workshop were published and widely disseminated under the general series title *Medical Innovation at the Crossroads*.⁴

The Conference on “Medical Innovation in the Changing Healthcare Marketplace” highlighted many of the key factors that either foster or inhibit medical innovation. Two particular areas seem to us to warrant further attention. One is finding ways to improve the diffusion of high-value innovation, and the other is to identify ways to foster the development of a much more sophisticated, yet affordable, health care information infrastructure.

During the conference David Lawrence of Kaiser Permanente reported on how the IOM Roundtable on Health Care Quality documented three types of quality problems—underuse, overuse, and misuse. With regard to underuse the Cochairs of the Roundtable commented,⁵ “Failure to use effective treatments (e.g., thrombolytics, beta-blockers, aspirin, and angiotensin-converting enzyme inhibitors) for acute myocardial infarction for all

¹National Research Council. 1999. *U.S. Industry in 2000: Studies in Competitive Performance*. Washington, D.C.: National Academy Press.

²Linda T. Kohn, Janet M. Corrigan, and Molla S. Donaldson, Editors; Committee on Quality of Health Care in America, Institute of Medicine. 2000. *To Err Is Human: Building a Safer Health System*. Washington, D.C.: National Academy Press.

³Committee on Quality of Health Care in America, Institute of Medicine. 2001. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, D.C.: National Academy Press.

⁴Institute of Medicine. 1990, 1991, 1992, 1994. *Medical Innovation at the Crossroads*. Washington, D.C.: National Academy Press.

⁵Chassin, Mark R., Robert W. Galvin, and the National Roundtable on Health Care Quality. 1998. The urgent need to improve health care quality. *JAMA* 280(11):1000-1005.

patients who could benefit from these interventions may lead to as many as 18,000 preventable deaths each year in the United States.” Given the documented underuse of some medical technologies and the documented overuse of other medical technologies, several speakers at the conference questioned whether the right incentives are in place for the diffusion of high-value innovation. We believe that, rather than addressing the issue of incentives directly, a better understanding is required of all aspects of the diffusion process. The incentive structure may not be the only, or even the dominant, factor affecting the diffusion of high-value medical technology. As a result, we believe that a better understanding is needed of the drivers of and barriers to the diffusion of medical technology in order to identify the public policy levers that could foster the rapid diffusion of high-value medical innovation and limit the use of low-value technologies.

As has been observed before, the health care delivery industry invests in information technology much less than other information-intensive industries. On the basis of the presentations and discussions at the conference, we believe there are opportunities to add value in this area. One is to investigate how to integrate the thinking of production management and quality control into the health care delivery system. Such thinking is a necessary precursor to the acquisition of information technology in the health care delivery system. Another opportunity is to examine how government has stimulated the development of infrastructures in the fairly recent past to help develop a model for government stimulation of a much more advanced information infrastructure for health care delivery. Examples include the interstate highway system, the health care facility program (Hill-Burton Act), the Superfund, and the Internet.

This document summarizes the conference presentations. From the outset, the committee recognized that the conference could never comprehensively cover the subject of medical innovation. As a result, many issues such as reimbursement barriers to innovation, cooperation among government agencies regarding medical innovation, the impact of direct-to-consumer advertising, and how to deal with the bureaucratic burden imposed on the health care industry were only partially explored.

Further, this report is not intended to be a comprehensive report on the presentations. This is available on the Web (www.nationalacademies.org/med_innovations) through the transcripts of the presentations and the speakers’ PowerPoint presentations.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council’s Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional

standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report: Robert M. Califf, Duke University Medical Center; Molly J. Coye, The Health Technology Center; David M. Cutler, Harvard University; Joseph V. Simone, Simone Consulting; and Ellen Stoval, National Coalition for Cancer Survivorship.

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by Richard A. Rettig, RAND Corp. Appointed by the National Research Council, he was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

Finally, we would like to thank the other members of the committee for their valuable advice on the issues that should be addressed at the conference, their analyses of the issues raised at the conference, and their suggestions for initiatives that could foster high-value medical innovation. We would also like to thank the staff of the Board on Science, Technology, and Economic Policy and of the Board on Health Care Services for their support throughout the project.

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Executive Summary

This document reports on the Conference “Medical Innovation in the Changing Healthcare Marketplace,” held June 14–15, 2001, Washington, D.C., at the National Academy of Sciences.

THE AIM OF THE CONFERENCE

The overarching question addressed by the conference was:

In an environment of renewed concern about rising health care costs, where can public policy stimulate or remove disincentives to the development, adoption and diffusion of high-value innovation in diagnostics, therapeutics, and devices?

This question was addressed both at the macro level and at the disease-specific level. Two contrasting diseases were discussed at the conference—cardiovascular disease and metastatic melanoma. For cardiovascular disease, there have been major advances in acute care, drugs, devices, and preventive measures over the last half-century, and these have resulted in significantly reduced morbidity and mortality. In contrast, for metastatic melanoma, there has, to date, been very limited therapeutic progress and the impact on morbidity and mortality has been slight.

The conference presentations addressed four main themes—characteristics of medical innovation, costs and benefits of medical innovation, cost-effectiveness studies and innovation development, and barriers to medical

innovation. The key points made by conference speakers with regard to these themes are summarized in the next four sections.

THE CHARACTERISTICS OF MEDICAL INNOVATION

Conference speakers made two important observations about the characteristics of medical innovation. First, innovation in diagnostics, therapeutics and devices are important but are not the whole story. Corresponding innovations in the health care delivery system have not taken place and are badly needed if the full benefits of innovations in diagnostics, therapeutics and devices are to be achieved. The broad range of these innovations since World War II has led to an enormous growth in the complexity of health care. However, the health care delivery system has not evolved to accommodate this complexity. Sophisticated delivery systems are lacking. There has been inadequate investment in information processing systems, and there has been insufficient emphasis on teamwork in care delivery. The inadequate investment in information processing systems led one speaker at the conference to say that there is a need for the federal government to take a leadership role in fostering a health care information infrastructure.

The second important observation was that innovation in implanted devices and drugs follow quite different paradigms. The former are much more likely to undergo improvements leading to significant cost-effectiveness improvements over time. For example, improvements in the technology of implantable cardioverter defibrillators (ICDs) and the way they are deployed have reduced the average cost of a life-year saved from about \$50,000 in the mid-1980s to less than \$20,000 in the early 1990s (Stanton et al., 2000). As a result of such improvements, early cost-effectiveness studies for devices are likely to present worst-case scenarios and could lead to premature abandonment.

THE COSTS AND BENEFITS OF MEDICAL INNOVATION

With health care costs once again increasing faster than general inflation, attention has focused on medical innovation being a driver of health care costs. According to researchers at the Centers For Medicare and Medicaid Services (CMS),⁶ medical innovation has been the primary driver of health care costs over the second half of the 20th century. It has accounted for about half the real growth in health care spending over the period 1950–2000, with the other half being attributable to factors such as the

⁶Formerly, the Health Care Financing Administration (HCFA).

aging population, increasing disposable income, and expanding insurance coverage.

Aggregate pharmaceutical costs have increased much faster than overall health care costs in recent years. Examination of the drivers of aggregate pharmaceutical costs shows that increased use of existing drugs is a more important driver than the use of new drugs, while unit price increases of existing drugs have been very similar to increases in the overall Consumer Price Index for all goods and services. In 2000, pharmaceutical spending was 13.6 percent higher than in 1999. Of this increase, 3.9 percentage points can be attributed to unit price increases of existing products, 7.5 percentage points to increases in the utilization of existing products, and the remaining 2.2 percentage points to the use of new drugs (IMS Health, 2001). Other recent year-on-year increases have shown a similar pattern.

Increasing use of existing drugs is the result of the treatment of more patients and the application of new science (Dubois et al., 2000). More people are being treated because the population is aging and there is a narrowing of the gap between prevalence rates and treatment rates for many diseases. Further, science is identifying new ways of using existing drugs. Increased use of prescription pharmaceuticals also reflects in part a greater understanding of their value offsetting other health care costs (Lichtenberg, 1996, 2001) and improving workplace productivity (Kessler et al., 2001).

The debate about health care largely focuses on its costs as though its benefits have little or no value, which is far from the case. One speaker estimated the social benefit of medical research by placing a value on aggregate improvements in longevity. To do this he first estimated the average amount an American would pay to add an extra year to his/her life. Using data on what workers are paid in occupations with differing risks of job-related death, the speaker estimated the value of an additional life-year to be about \$150,000, a figure that varies with age. Using these age-dependent values of an additional life-year he estimated that increased life expectancy over the period 1970-1990 is valued at roughly \$57 trillion or about \$2.8 trillion per year (Viscusi, 1993; Tolley et al., 1994; Cutler et al., 1998; Cutler and Richardson, 1999; Lasker Foundation, 2000; Topel and Murphy, Forthcoming). Expressed another way, over the period 1970-1990, improvements in life expectancy have contributed about as much to overall welfare as have improvements in material wealth.

Another speaker showed that the returns on investment in medical technology for cardiovascular disease applications are very significant. For someone 45 years old, half of the 9-year increase in life expectancy over the period 1950-2000 is a result of reduced cardiovascular disease mortality. The speaker attributed roughly two thirds of the cardiovascular benefits (3 extra years) to improvements in medical treatment and roughly one third

(1½ extra years) to behavioral changes. Based on the average cost of medical treatment for cardiovascular disease and the cost of providing behavioral advice, and assuming that an extra year of life is valued at \$100,000, the speaker demonstrated that the return on medical care is very high, about 4:1, and the return on behavioral changes is much higher, about 30:1.

In the context of escalating costs associated with innovation, one speaker concluded that new technologies (most of which tend to be expensive—for example, Left Ventricular Assist Devices for heart failure) and the aging of the U.S. population are going to drive up the costs of cardiovascular care. He doubted whether new technologies would improve efficiency on the grounds that the U.S. system is too fragmented to take advantage of money-saving innovations.

Again, in the context of escalating costs associated with innovation, the lack of CMS reimbursement may significantly curtail the development of promising therapeutic agents. For example, high dosage Interleukin-2 (IL-2) is the only effective treatment for metastatic melanoma, but only for a small subset of patients. Criteria for predicting this responsive subset are currently lacking. High dosage IL-2 is a very costly in-patient therapy with CMS only reimbursing a fraction of the total cost. Some major centers do not offer this therapy, even for those who are able to pay for the treatment. The lack of full reimbursement, allied to the unpredictable outcome of the treatment, has curtailed research efforts to improve the therapy.

COST-EFFECTIVENESS STUDIES AND INNOVATION DEVELOPMENT

Cost-effectiveness studies for a new medical technology are often crucial to the development of that innovation. Three case histories were presented at the conference—tissue plasminogen activator (t-PA) and implantable cardioverter defibrillators (ICDs)—where cost-effectiveness studies encouraged diffusion and one—intravascular ultrasound (IVUS)—where cost-effectiveness studies discouraged diffusion.

Two trials in Europe found that the mortality rates for administering t-PA or streptokinase after a heart attack were identical. At the time, t-PA cost about \$2,200 per treatment, while streptokinase cost about \$300. Subsequently, the market share of t-PA in the United States began to slide. This led Genentech to fund a very large U.S. trial (GUSTO-1) that found that t-PA had a better mortality rate than streptokinase. Later analysis of the trial data (Mark et al., 1995) showed that t-PA provided an extra life year at a cost of \$33,000. Recombinant thrombolytics (t-PA and others) now account for 96 percent of the U.S. market.

One of the early barriers to the adoption of ICDs was the lack of cost-effectiveness studies. Eventually, randomized controlled trials (RCTs) were carried out comparing the use of ICDs with the best available drug. The results (Connolly et al., 2000) showed that patients given ICDs had a 28 percent lower chance of dying from all causes. This was convincing evidence that ICDs enabled patients to live longer.

IVUS was developed by academic cardiologists in the late 1980s and was approved by the FDA in the early 1990s. IVUS is currently used as a diagnostic and research tool. Cost-effectiveness data (Berry et al., 2000) showed that broad use of IVUS in angioplasty was not justified. Development and widespread use of the technology have, as a result, been limited.

In contrast to the above technologies, many technologies are poorly assessed for cost-effectiveness prior to use. For the diagnosis of melanoma, examples discussed at the conference were digital imaging, epiluminescence microscopy, and qualitative image analysis. This lack of objective assessment is ascribed to the passivity of payers of health care services. At the same time, physicians and patients have been aggressive about demanding the latest technology, while Congress and the courts are reluctant to control access to new medical technologies. Against this background, two speakers believed that payers should take a more active role in clinical trial design and fund key trials. In this regard, Medicare has recently started to pay for the routine costs of care in clinical trials, but so far has paid for only two trials.

BARRIERS TO THE DEPLOYMENT OF HIGH-VALUE INNOVATION

The conference discussed a wide range of barriers to the deployment of high-value innovation at the technical level, at the public policy level, and in the broader political context. In considering barriers to innovation, it should be noted that not all stakeholders see each barrier in the same light. For example, regulations may be seen by some as inhibiting the deployment of technology and by others as providing important safeguards.

Technical level barriers that were discussed included inadequate understanding of the biology of cancer, poorly predictive pre-clinical models for cancer therapies,⁷ inadequate effort devoted to cost-effectiveness analyses, and a shortage of patients willing to participate in clinical trials.

Public policy barriers were discussed at some length at the conference. The following are the key barriers that were identified:

⁷It should be noted that many other major diseases, such as heart disease, stroke, and depression, also have poor pre-clinical models.

- Reimbursement policies not friendly to innovation. The IOM Roundtable on Health Care Quality (Chassin et al., 1998) documented the extensive underuse and overuse of medical technologies. This suggests that the right incentives for the diffusion of quality care may not be in place. Furthermore, two speakers pointed out that fee-for-service payment methods, originally designed for short-term acute care, reward individual acts by individual people. They do not support well-integrated delivery capabilities increasingly necessary to treat a wide range of chronic conditions.

- Inability of federal agencies to cope in the face of a significant increase in the amount and a broadening in the scope of medical innovation. A factor that could have an important bearing on the FDA's ability to cope will be the post-September 2002 arrangements for paying user fees for New Drug Applications.

- Excessive regulation inhibiting change and costly to implement. For example, CMS has 130,000 pages of rules, regulations, and guidelines. Kaiser Permanente has estimated that between 5 and 7.5 percent of total annual revenues are devoted to meeting local, state, and national regulatory requirements.

- Public policy changes, a major uncertainty for venture capitalists. Although venture investors are able to evaluate technology and development risks, it is more difficult to anticipate the impact of public policy changes that may extend the period of development and increase its cost (for example, by regulation) or reduce returns on investment (for example, by price controls).

- Older public policies may no longer provide the right incentives. The Orphan Drug Act of 1983 and the Waxman-Hatch Act of 1984 were enacted in the early days of the biotechnology industry, and the incentives written into these two laws may not now be economically relevant.

- Rules for managing conflicts of interest may end up inhibiting innovation. One speaker said that concerns about conflicts of interest had become pervasive, particularly in academic medical centers. The speaker believed that attempts to legislate honesty and integrity would not work. Moreover, he feared such rules might inhibit innovation.

Several conference speakers pointed to the potential negative impacts on medical innovation of some broader political and economic trends:

- Congressional reluctance to address health care issues. Congress has understandably become reactive to health care issues because the issues are complex, political capital is difficult to gain from health care legislation, and congressional opinion is fragmented on health care issues. Areas where congressional leadership would be important include establishing incen-

tives for the delivery of quality care and fostering investment in information technology in the health care delivery system.

- Increasing scrutiny of health care prices could influence return on capital. Politicians, employers, insurers, and providers are reluctant to make choices on behalf of consumers/patients about their health care. By default, consumers will have to make more of the choices (Robinson, 2001), balancing quality of care choices against out-of-pocket expenses. Moreover, almost certainly they will have to assume more of the cost burden, leading to further scrutiny of health care costs. The resulting downward pressure on prices could reduce investors' return on investment. On the other hand, better-informed consumers may demand more services, resulting in an expansion of the market.
- Lack of responsiveness to equity issues might reduce public support for federal funding of medical research. Too large a proportion of the population without insurance coverage or too large a proportion of the insured lacking prescription insured coverage could undermine political support for high levels of NIH funding.

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Introduction

Medical innovation has contributed enormously to the improvement of the health of the American people, especially to the increase in life expectancy over the past 50 years. At the same time, aggregate health care costs have grown much faster than the overall economy. As Mark McClellan of the Council of Economic Advisers pointed out in his introductory address, medical innovation is at a public policy crossroads. On the one hand, there is strong pressure to develop innovative medical technologies, while on the other hand, there are growing concerns about the economic implications of medical innovation. In McClellan's view the critical questions is:

In an environment of renewed concern about rising health care costs, where can public policy stimulate or remove disincentives to the development, adoption, and diffusion of high-value innovation in diagnostics, therapeutics, and devices?

To address this question, the Board on Science, Technology, and Economic Policy and the Board on Health Care Services organized a conference at the National Academies headquarters on June 14–15, 2001.

THE CONFERENCE AGENDA

The first half of the conference addressed two key aspects of the public policy debate about new medical technology—the extent to which new medical technology is driving up health care costs and the challenge of

putting a value on the benefits of new medical technology. These two issues were addressed at the macro level and at the disease level for cardiovascular disease⁸ and metastatic melanoma.⁹ The conference agenda is in Appendix A.

In choosing these two diseases, the organizers of the conference sought to contrast the situation for a disease where there has been significant therapeutic progress, cardiovascular disease, with the situation for a disease with, to date, limited therapeutic progress, metastatic melanoma.¹⁰ Indeed, metastatic melanoma can be considered representative of many cancers in the sense that new drugs are becoming available that provide improvements but at substantial cost.

The second half of the conference addressed the impact of innovations in the pipeline and the barriers to these innovations. Barriers to innovation occur at all stages of the innovation cycle—development (potentially exciting ideas that do not leave the drawing board), adoption (coverage denied or delayed for cost-effective solutions), and diffusion (proven solutions only slowly replacing inferior approaches). Ways to overcome identified barriers to medical innovation were considered with respect to treatments for cardiovascular disease and for metastatic melanoma, as well as more generally.

Chapters 2–5 of this report summarize the discussion of the four principal themes of the conference:

- The characteristics of medical innovation.
- The costs and benefits of medical innovation.
- Cost-effectiveness studies: a key to innovation development.
- Barriers to medical innovation.

A list of conference participants is given in Appendix B. This list does not include those people who tuned into the conference webcast, which drew about 100 listeners each day.

⁸Cardiovascular disease, principally heart disease and stroke, is the leading cause of death in the United States for both men and women among all racial and ethnic groups. More than 960,000 Americans die of cardiovascular disease each year, accounting for more than 40 percent of all deaths. In addition, about 58 million Americans live with some form of cardiovascular disease.

⁹Melanoma is a malignant tumor that begins in the cells that produce skin coloring (melanocytes). When melanoma cells spread beyond the initial site to other parts of the body (for example, lymph nodes, liver, lungs) the disease is called metastatic melanoma. The incidence of melanoma in the United States is increasing. It is estimated that in 2001 about 51,000 new cases of melanoma will be diagnosed and about 7,800 deaths will be attributed to the disease.

¹⁰It should be noted that other cancers (for example, cancers of the lung, bronchus, and pancreas) also have very low 5-year survival rates.

A transcript of McClellan's speech and the subsequent discussion appears in Appendix C. David Lawrence, chief executive officer of Kaiser Permanente, delivered the opening address on the second day of the conference. A transcript of his speech and the subsequent discussion appears in Appendix D.

The Characteristics of Medical Innovation

Conference speakers made two important points about the characteristics of medical innovation. First, innovations in diagnostics, therapeutics, and devices are important but are not the whole story. Corresponding innovations in the health care delivery system have not taken place. David Lawrence and Jerry Grossman of the Lion Gate Management Corporation and the Kennedy School of Government both emphasized the need for innovations in the health care delivery system if the full benefits of innovation in diagnostics, therapeutics, and devices are to be achieved. Second, innovation in implanted devices and drugs follow quite different paradigms. Paul Citron of Medtronic observed that the former are much more likely to undergo improvements leading to significant cost-effectiveness improvements over time. As a result early cost-effectiveness studies for implanted devices are likely to be worst-case scenarios and could lead to premature abandonment of the technology.

MEDICAL INNOVATION SHOULD NOT BE TOO NARROWLY DEFINED

Grossman and Lawrence both emphasized that “the tools of care” have far outstripped “the tools of caring.” Innovations in diagnostics, therapeutics, and devices have moved far faster than the tools for delivering these breakthroughs. As a consequence, innovation in delivery systems is badly needed if the full benefits of innovation in diagnostics, therapeutics, and devices are to be achieved.

Lawrence observed that the vast array of medical innovations since World War II has led to a tremendous growth in the complexity of health care. The health care sector has not evolved to accommodate this complexity. In other sectors where complexity had significantly increased, sophisticated production systems have been implemented, an information technology infrastructure installed, and teamwork developed.

In medicine, these types of developments have not occurred in the health care delivery side. Production design is a foreign word. It is estimated that between 1 and 2 percent of total revenues in health care are invested in information technology—well below the level of investment in other information-rich industries. Physicians are still imbued in training with the principle of individual, professional autonomy despite the fact that most practitioners are not working in autonomous situations.

Funding information technology investments is a big problem. As McClellan commented it may be that the financial rewards for good information systems in the health care delivery industry are significantly lower than they are in other industries. Privacy concerns are also a barrier to investment in health care information systems.

Lawrence thought that there may be a role for the federal government in the development of the health care information infrastructure. He believed that Singapore might be showing the way through the creation of an investment pool for information technology experiments. He had in mind a federally sponsored investment bank that would be experiment- and innovation-driven. This bank would fund a number of major experiments and from these we would learn about how best to establish a health care information infrastructure.

DEVICES AND DRUGS ARE DIFFERENT IN THEIR COST-EFFECTIVENESS OVER TIME

Paul Citron said that the paradigms for implanted medical device innovation and drug innovation are quite different. Devices provide site-specific therapy and exhibit a direct mechanism while drugs act systematically and have an indirect mechanism of action. As a consequence, device therapy has fewer side effects than drugs. Further, devices incur a high initial cost at implantation that is amortized over the service life of the therapy, whereas the costs of drug therapy accumulate and can be substantial over the treatment period. Another key distinction is that devices undergo continuous evolutionary improvements usually with cost-effectiveness improvements while cost-effectiveness for drugs remains relatively constant.

Improvements in the cost effectiveness of devices can be intrinsic—technological improvements in the device—or they can be extrinsic—improvements in the way the technology is deployed. Examples of intrinsic

improvements are pacemaker internal current requirements and pacemaker functionality. In the 1960s and early 1970s, pacemakers were made of discrete components and required 30 micro-amps (late 1960s) and 22 micro-amps (early 1970s) to operate. Modern devices use integrated circuits and energy consumption has been reduced to about 4 micro-amps (Ohm, 1997). Thus, over the last 30 years there has been a seven-fold improvement in the internal operation of the device. In terms of pacemaker functionality, early devices stimulated the heart once a second whether it needed to be stimulated or not. Modern pacemakers are computers that constantly monitor the underlying heart beat rhythm and make adjustments as appropriate. In addition, the pacemaker stores data on what the device has done to help the cardiologist understand how the patient is progressing.

Combining intrinsic technology advances and extrinsic factors has progressively improved ICD cost-effectiveness (Stanton et al., 2000):

- Around 1985, ICDs required open-chest implantation. Morbidity was about 5 percent. The batteries had a 2-year life expectancy. These first generation ICDs were judged to be marginally cost-effective at just under \$50,000 per life year saved.
- Shortly afterwards, the battery life was extended to 4 years, and cost effectiveness improved to just under \$40,000 per life-year saved.
- In the early 1990s, a paradigm shift occurred. Transvenous electrodes were developed that required less invasive surgery. Morbidity was reduced and the length of stay in the hospital was shortened. The average cost per life saved was further reduced to under \$20,000.
- The ICD might now be a cost-saving technology because the sensing devices built into the ICDs can now monitor and correct automatically some cardiac rhythm disorders that previously would have required a hospital visit.

Citron concluded by saying that early cost-effectiveness studies for devices are likely to present worst-case scenarios and could cause a device to be abandoned prematurely.

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The Costs and Benefits of Medical Innovation

An era of health care cost containment has come to an end. Once again concerns are expressed about rising health care costs and medical innovation is seen as an important driver of health care costs. Two presentations at the conference directly addressed the extent to which medical innovation drives up health care costs. One presentation looked at increases in total spending over the past 50 years, and the other looked at recent increases in aggregate prescription drug spending over the last few years.

There appears to be much greater emphasis in the public debate on the costs than the benefits of health care. An example of this perspective is a Washington Post editorial (Washington Post, 2001) “Back to Health Care Costs” published shortly before the conference. It stated:

Higher health care costs are like a tax increase or an increase in energy costs. They leave people, businesses and government—government in its role as major payer of medical bills—with less money to spend for other purposes.

The editorial focused on costs as if all health care expenditures are investments that evaporate and do not bring any value to the population. To redress the balance, several presentations sought to place a value on the benefits of medical innovation.

Finally, four speakers examined some recent developments in treating cardiovascular disease and metastatic melanoma and the cost implications of these developments.

ACCORDING TO CMS RESEARCHERS, TECHNOLOGY IS PRIMARY DRIVER OF HEALTH CARE COSTS

Researchers at CMS find that technological change has been the largest single driver of growth in health care spending over the past 50 years.

An estimated \$4,660 per person was spent on health care in 2000—an increase of 838 percent from the \$497 spent in 1950, assuming constant dollars. Sheila Smith, an economist with CMS, sought to evaluate the contribution of technological change, aging, insurance coverage, and other factors to historical growth in real per capita health care costs. Her approach was to identify the nontechnological factors contributing to growth in health spending and then to estimate their contribution, given a constant state of medical technology. The residual growth is then attributed to medical technology. The nontechnological factors taken into account included demographic factors (population growth and aging), relative medical price inflation, rising insurance coverage, increasing disposable income effects, supplier-induced demand and avoidable administrative costs. The last factor is defined to be the unnecessary costs associated with institutional structures within the health care sector.

After taking account of all these nontechnological factors, the residual implies that approximately 2.2 percent annual growth in real per capita health spending can be attributed to technology—the estimation range is 1.9 to 2.9 percent. Expressed another way, technological change has accounted for about half the real growth in health care spending over the period 1950-2000. This estimate of the impact of technological innovation is in line with earlier studies (Newhouse, 1992; Cutler, 1995).

INCREASED USE OF EXISTING DRUGS IS MOST IMPORTANT DRIVER OF AGGREGATE DRUG COSTS

Much attention in recent years has been devoted to increases in aggregate prescription pharmaceutical cost, even though prescription pharmaceuticals constitute only a small share of total health costs, less than 10 percent. Alison Keith, until recently an economist with Pfizer, Inc., examined the 13.6 percent increase in pharmaceutical spending in 2000 over 1999 (IMS Health, 2001):

- Unit price increases of existing products accounted for 3.9 percentage points—not very different from the increase in the overall Consumer Price Index for all goods and services.
- The biggest component, 7.5 percentage points, is attributable to increases in utilization of existing products.

- The remaining component, 2.2 percentage points, is attributable to the cost of new products.

Keith explained that other recent years show a similar pattern and that this increased volume of pharmaceutical utilization arises primarily from treating more patients and applying new science (Dubois et al., 2000):

- More patients—reflecting an aging population with more chronic conditions and co-morbidities, and a narrowing of the gap between prevalence rates and treatment rates for many diseases, in part due to a more widespread awareness of specific conditions and better detection and diagnosis.
- New science—encompassing new understanding of disease processes and the importance of specific treatments, and new best practices in the clinic.

Keith suggested that this increased utilization can be understood to reflect a greater recognition of the value of prescription pharmaceuticals, where their direct costs are viewed in the light of both health and economic contributions, which often include offsets in other health care costs (Lichtenberg, 1996, 2001) and improvements in workplace productivity (Kessler et al., 2001).

THE VALUE OF INCREASED LIFE EXPECTANCY OVER 1970–1990 IS ENORMOUS

University of Chicago economists Kevin Murphy and Robert Topel sought to evaluate the social benefits of medical research by placing a value on aggregate improvements in longevity (Viscusi, 1993; Tolley et al., 1994; Cutler et al., 1998; Cutler and Richardson, 1999; Lasker Foundation, 2000; Topel and Murphy, Forthcoming). The first task was to estimate what an average American would agree to pay for a reduction in mortality risk that would add a year to his/her life. Murphy and Topel used data on what workers are paid in occupations with differing risks of job-related death to estimate the value of an additional life-year to be about \$150,000, a figure that varies with age.

Over the period 1970–1990 increases in the life span of an average American have been significant. For example, the increase in the life span of a typical 40-year-old person is more than three years. Using age-dependent values of an additional life-year and the increases in life expectancy over this period, Murphy and Topel attribute a value of roughly \$57 trillion or about \$2.8 trillion per year to the increased life expectancy, indicating the public values improvements in health very highly. To put these figures

in perspective, improvements in life expectancy over the period 1970–1990 contributed about as much to overall welfare as did improvements in material wealth.

Kevin Murphy pointed out that investment in medical research has brought significant returns. In 1995, according to NSF calculations there were about \$35 billion in investments in medical research. The gain in health, as measured by the value of added longevity, is about 50-100 times what we spend on research, even taking into account the fact that health improvements are due to a variety of factors.

Looking forward, Murphy said that potential future gains will also be very large. For example, eliminating cancer is worth roughly \$47 trillion. Further, the economic value of disease reduction is increasing significantly over time. The value of disease reduction rises as the wealth of the population increases. In addition, the value of progress against any one disease rises as we make progress against other diseases. For example, as we have made progress against heart disease and, hopefully, make progress against cancer, the value of curing/mitigating Alzheimer's disease increases. The reverse is also true. Progress against Alzheimer's disease makes further progress against cancer or heart diseases much more attractive because of a better life in those later years as well as more years to live.

MAJOR RETURNS ON INVESTMENT IN MEDICAL TECHNOLOGY FOR CARDIOVASCULAR DISEASE

David Cutler, a Harvard University economist, explained that life expectancy has increased 9 years since 1950 with about half of this increase resulting from reduced mortality from cardiovascular disease. These successes in treating/preventing cardiovascular disease can be attributed to developments in the intensive treatment of heart attacks, new medications for chronic heart disease (hypertension, cholesterol, angina), and behavioral changes (less smoking, reduced fat intake, decline in heavy drinking). These developments, including the behavioral changes, are products of medical research.

To determine the return on medical care and basic research (Cutler, Forthcoming), Cutler attributed roughly one-third of the benefits to developments in intensive treatment, roughly one-third to new medications, and the remaining third to behavioral changes. For someone 45 years old the total increase in longevity is about 5 years since 1950, of which about $4\frac{1}{2}$ years is a result of reduced cardiovascular disease mortality, with 3 years from medical treatments and $1\frac{1}{2}$ years from behavioral changes. For someone 45 years old the average cost of medical treatment on cardiovascular disease is \$30,000 in present value terms. The costs of providing behavioral advice are much less—David Cutler estimated about \$1,000 to

cover the costs of research and consultation with health care professionals. For the purpose of estimating benefits, Cutler assumed an extra year of life to be worth \$100,000.¹¹

For the return on medical care, there is a cost of \$30,000 in exchange for three extra years. These three extra years are not valued at \$300,000 but at \$120,000 because some of the benefits occur in the future and need to be discounted. Even so, the return for medical care is very large, on the order of 4 to 1. For the return on behavioral changes, there is a cost of \$1,000 in exchange for just over an extra year. The discounted value of this extra time is \$30,000. Thus, the return on behavioral changes (30:1) is much higher than the return for medical care.

SIGNIFICANT POTENTIAL BENEFITS FROM MELANOMA PREVENTION PROGRAMS

As Cutler pointed out in his presentation, life style changes have brought about significant reductions in cardiovascular deaths. Life style changes can also have an impact on the incidence of melanoma. Margaret Tucker of the National Cancer Institute said that although the incidence of melanoma is increasing, it is a disease that can be prevented by decreasing sun exposure. To achieve this, major cultural issues need to be addressed since having a tan is an important part of “looking healthy” in American culture. These cultural problems have been successfully addressed in Australia where considerable investment in a prevention program has resulted in melanoma incidence rates leveling off, possibly even decreasing. The Australian program taught the need for sunscreens and protective clothing and led governments to provide shade at nearly all outdoor pools and school playgrounds.

Tucker also said that secondary prevention/early detection is practicable. In Australia, it has been estimated that a family practitioner doing a 2-year screening for adults over 50 costs about \$12,000 per male life-year saved, and \$21,000 per female life year saved (Carter et al., 1999). In America, it has been estimated that a one-time screen by a dermatologist with treatment would cost \$29,000 per life year saved (see below). These costs would decrease for targeted screening.

Robert Young of the Fox Chase Cancer Center said that screening for melanoma is still controversial primarily because it has not been fully assessed through a randomized control trial (RCT). Nevertheless screening is widely carried out. The American Academy of Dermatology, the American Cancer Society, and the NIH Consensus Conference all endorse regular

¹¹Note: this figure is somewhat lower than the figure (\$150,000) used by Kevin Murphy, above.

screening, while the Canadian task force on periodic health examination endorses screening for high-risk patients. On the other hand, the U.S. Preventive Services Task Force and the International Union Against Cancer do not endorse screening.

The issue of whether screening is cost-effective was addressed in a recent study by Freedberg et al (1999). This study examined whether no screening or a single one-time screen by a dermatologist could be cost effective for high-risk patients. The study found that it is cost-effective but highly dependent on the initial cost. If the screen costs \$30 then the cost per life year saved is \$29,170. However, if the screen costs \$120 then the cost per life year saved is \$110,000, a considerably higher figure whose acceptability is debatable.

In response to a comment that there is under investment in prevention research funding as compared to diagnostics/treatment research funding, Mark McClellan of the Council of Economic Advisers speculated whether the right reimbursement incentives were in place. Health care providers are generally paid more for doing more, for treating complications, and for treating the consequences of poor preventive care. John Ford, of the House Committee on Energy and Commerce minority staff speculated that the perceived under-funding of prevention research might move Congress to encourage more innovation in the area of prevention.

LOOKING TO THE FUTURE: COSTS OF TREATING CARDIOVASCULAR DISEASE LIKELY TO RISE

In a presentation on the future costs of treating cardiovascular disease, Dan Mark of Duke University observed that heart failure is a very important epidemic condition in the United States. As age-specific mortality is falling in cardiovascular disease the incidence of heart failure may be increasing. About 4.7 million people in the United States now have heart failure and a little over half a million new cases are added each year. The treatment options are palliating the symptoms, drugs that improve the prognosis, disease management (a low-tech collaborative approach), or attempting to reverse the heart failure state. The latter could involve giving the patient a new heart or inserting a Left Ventricular Assist Device (LVAD), a mechanical device similar to an artificial heart that is designed to increase the efficiency of the cardiovascular system.

Currently, about 2,300 heart transplants are carried out a year in the U.S. at a lifetime cost of about \$300,000 per patient, resulting in an annual expenditure of \$700 million. The number of heart transplants is limited by the total number of donated hearts. This has been stable for a number of years and is unlikely to increase anytime in the future. If an LVAD could be used instead of a heart transplant then potentially another 40,000–50,000 patients could benefit from such a device.

Currently, LVADs are approved as a bridge to a heart transplant to keep severe heart failure patients alive as they await for a transplant. LVADs cost in the range \$50,000-75,000 excluding the costs of implantation and maintenance. If LVADs move from “bridge to transplant” use to standalone left ventricular support use not necessarily anticipating transplant then the device could have a huge economic impact. If the costs for LVADs were in the range \$100,000-200,000 then that would add \$5 billion-10 billion to annual health care costs. An ongoing clinical trial is testing this strategy. Its outcome is uncertain, but there is certainly the potential for explosive growth in the cost of the care of patients with heart failure.¹²

Mark concluded by saying that new technologies, most of which tend to be expensive (for example, LVADs for heart failure), and the aging of the U.S. population are going to drive up costs of cardiovascular care. There is always the potential for new technology to improve efficiency but, in Mark’s view, the U.S. system is too fragmented to take advantage of money-saving innovations.

NEW THERAPIES FOR METASTATIC MELANOMA ARE EXPENSIVE

Mike Atkins of the Beth Israel Deaconess Medical Center, Harvard Medical School, reported on developments in the treatment of metastatic melanoma. He said the disease had a bad prognosis—a median survival of 6-10 months and less than 5 percent of patients survive 5 years. Traditional approaches to treating cancer—surgery, radiotherapy, and chemotherapy—have not been successful. Although chemotherapy can produce tumor shrinkage in a small percentage of patients, these responses are usually of short duration. Overall it is unclear whether chemotherapy produces a survival advantage over simple observation. Clinical cost-effectiveness is very low.

Immunotherapy is currently the most promising therapy for metastatic melanoma. High dosage Interleukin-2 (HD IL-2) is very effective for a small subset of patients. Criteria for identifying this responsive subset are currently lacking. HD IL-2 is, however, costly and requires in-patient delivery. Typical costs per patient are \$52,000, and CMS only reimburses up to \$18,000. As a result, some major centers do not to treat metastatic melanoma patients, even those who can afford to pay for themselves. In addi-

¹²After the conference, the results of the REMATCH trial were published (see Rose et al. 2001. Long-term Use of a Left Ventricular Assist Device for End-stage Heart Failure. *N. Eng. J. Med.* 345(20):1435-1443.) showing the benefit of the left ventricular assist device in reducing mortality and improving quality of life in end-stage heart failure patients.

tion, research efforts to improve IL-2 therapy have been hampered or even curtailed.

Bruce Hillner of the Medical College of Virginia reported on a study (Hillner et al., 2001) that confirmed the high cost of current treatments for metastatic melanoma. The study reported on an audit of the records of 100 consecutive new patients with metastatic melanoma at the University of Pittsburgh Cancer Institute (UPCI) after January 1997. An exceptionally high proportion (84 percent) of the group of patients participated in clinical trials—49 percent in Phase I trials, 10 percent in Phase II trials, and 25 percent in Phase III trials. In terms of therapies, 75 percent of the group received immunotherapy, 50 percent chemotherapy, 44 percent radiotherapy, and 23 percent surgery. Using assigned costs for the identified resources, the average cost per patient was \$59,400. This figure represents a lower bound on the costs of treating the disease, since it omits the diagnostic costs prior to referral to UPCI and the costs of supportive care at the end of life. At the time of the analysis 82 percent of the patients were known to have died.

SOME RECENT DEVELOPMENTS IN IMMUNOTHERAPY FOR TREATING METASTATIC MELANOMA

Steven Rosenberg of the National Cancer Institute reported on his work to develop peptide vaccine strategies in combination with other therapies for the treatment of metastatic melanoma. He said that in the last decade we have seen the development of a fourth approach (after surgery, radiation therapy and chemotherapy) to cancer therapy—immunotherapy or biologic therapy, aimed at stimulating the body's defenses to defeat cancer (Rosenberg, 2001). The use of IL-2 for in-patient treatment of metastatic melanoma and other cancers is the best example that immune stimulation can result in cancer regression. It is possible to incubate cancer cells in the highest achievable concentration of IL-2 and they will grow normally. All of the impact of IL-2 derives from its ability to stimulate the body's immune system.

To develop immunotherapy further, a molecular understanding of the process is needed, particularly, an identification of the antigens involved in cancer regression. Using tumor-infiltrating lymphocytes, first identified in the late 1980s, tumor antigens in melanoma and other cancers have been discovered. Rosenberg said that these discoveries have opened up opportunities for new approaches for treating cancer patients by using their own immune systems. For example, peptides that mimic tumor antigens can be used to vaccinate patients and evoke an immune response. In pilot trials, the response rate to IL-2 has been doubled using peptides in conjunction with IL-2. A nationwide RCT is now evaluating IL-2 as compared with

IL-2 plus peptide. Regarding the economics of this peptide treatment, Rosenberg said that under GMP (Good Manufacturing Practices) conditions synthesizing enough peptide to treat 1,000 patients costs about \$12,000.

Jonathan Lewis said that his company, Antigenics, is a relatively new biotechnology company specializing, among other things, in developing immunotherapy products.¹³ He said that building on the work of Pramod Srivastava and others, laboratory researchers had shown that treating animals with cancer with autologous tumor-derived heat shock protein molecules can generate an immune response leading to favorable results in terms of both survival and tumor regression. This had been demonstrated for a wide range of histologies and several different methods of inducing the cancer (see for example Tamura et al., 1997).

Lewis said that translating results in animals to humans is a big step. First, there is inadequate species molecular homology, in other words, humans are very different from mice. Second, laboratory experiments are carried out on very inbred strains of mice, whereas humans are very heterogeneous. These caveats are bypassed by heat shock protein biology. Researchers have demonstrated that it is possible to prepare heat shock protein vaccines for humans, that these vaccines are safe and tolerable for humans, and that the use of vaccines has elicited documented anti-tumor activity in humans. Regarding the latter point, in a recent uncontrolled trial carried out at the M.D. Anderson Cancer Clinic in which late stage and heavily pre-treated melanoma patients were given a heat shock protein vaccine, there was 95 percent survival at a median follow-up of 14 months in adjuvant patients, and 50 percent survival in residual disease patients.¹⁴ These were better results than had been previously seen at this center. A comparable study at the National Cancer Institute, Italy, showed similar findings.¹⁵ In addition, they saw some patients undergo a complete response, that is, all their cancer went away.

Lewis concluded by saying that studying and understanding melanoma will help gain a much better understanding of many other different types of cancer. For example, over the past year researchers at Antigenics had observed many important similarities between melanoma and renal and pancreatic cancer.

¹³Antigenics, Inc., announced on October 15, 2001, that its product, Oncophage®, had become the first personalized cancer vaccine to receive FDA Fast Track designation.

¹⁴These results were announced by Dr. Omar Eton of the M.D. Anderson Cancer Center in Houston at the annual conference of the American Association of Cancer Research in San Francisco, April 2000.

¹⁵These results were presented by Dr. Giorgio Parmiani of the Istituto di Tumori de Milano at the annual conference of the American Society of Clinical Oncology in San Francisco, May 2001.

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Cost-Effectiveness Studies: A Key to Innovation Development

Several speakers at the conference observed that outcome analysis/cost-effectiveness studies are often key to innovation development. Such studies can enhance development/diffusion, as was the case for t-PA (tissue plasminogen activator) and implantable cardioverter defibrillators (ICDs). They can also impede development/diffusion, as was the case for intravascular ultrasound (IVUS).

Robert Young of the Fox Chase Cancer Center pointed to the reluctance to carry out cost-effectiveness studies resulting in new technology being used without adequate cost-effectiveness assessment. Richard Pazdur of the Food and Drug Administration (FDA) outlined some of the evaluation challenges facing metastatic melanoma. Fran Visco of the National Breast Cancer Coalition described how a patients' advocacy group has fostered evidence-based medicine. Sean Tunis of the Center for Medicare and Medicaid Services (CMS) described the more formal approaches to coverage decisions now being adopted by CMS. Finally, Mark McClellan described a government initiative to develop a more seamless approval and coverage process.

TISSUE PLASMINOGEN ACTIVATOR (t-PA) CASE HISTORY

Dan Mark of Duke University began by saying that in terms of the economics of new therapies there are two key questions. The first question: is the new therapy good value for money? Expressed another way, is there an appropriate balance between the incremental health benefits that are

being produced and the incremental costs that are required to produce these benefits? If a therapy represents good value for the money, then the second question is whether there is money available to make the therapy generally available. Mark used the history of the development of t-PA (tissue plasminogen activator) to throw light on these two questions.

Mark outlined the development of thrombolytic therapy, streptokinase. In the 1980s, two very large RCTs were carried out in Europe to evaluate streptokinase. The ISIS2 trial was the second trial and was published in 1988. This trial showed that the combination of streptokinase therapy plus one aspirin taken in the emergency room lowered the mortality rate in heart attack patients from 13 percent to 8 percent. A paradigm shift in the treatment of heart attacks had been achieved. Instead of being a passive observer, cardiologists now had a therapy that could change the outcome for many heart attack patients.

Around this time Genentech developed recombinant t-PA. By 1985, the NIH had conducted the TIMI1 trial, which had shown that at 90 minutes after the onset of a heart attack the t-PA drug had twice as many open infarct arteries as the streptokinase drug. This was regarded as a major advance in the care of acute myocardial infarction patients. Treatment had gone from a low-tech bacterial enzyme (streptokinase) to a high-tech genetically engineered product (tissue plasminogen activator). In the United States, no trial was carried out to evaluate the mortality benefits of t-PA. Since the drug opened more arteries there seemed no question that patients would live longer.

In a more skeptical Europe, two large-scale trials, GC2 and ISIS3, were carried out. Both of these trials found that t-PA and streptokinase were equivalent in mortality rates. This was a shock to U.S. cardiologists and it had a serious negative effect on the market share of t-PA. At the time of the GC2 and ISIS3 trials t-PA had a U.S. market share of about 70 percent, with streptokinase having the remaining market share. t-PA's market share dropped to 55 percent and at this point Genentech decided to fund the GUSTO-1 trial comparing streptokinase with t-PA. This 40,000 patient trial showed that the streptokinase patients at 30 days had a 7.3 percent mortality rate and the t-PA patients had a 6.3 percent mortality rate. At the time the streptokinase treatment cost about \$300 while the t-PA treatment cost about \$2,200, a seven-fold difference in price. Subsequent cost-effectiveness analysis showed that t-PA provided an extra life year at an estimated cost of \$33,000 (Mark et al., 1995; Mark, in press). As a result of this analysis, t-PA was judged to be an economically attractive therapy. Recombinant thrombolytic agents (t-PA and others) now have 96 percent of the U.S. market with streptokinase having just 4 percent.

On a national level the economic cost of shifting from streptokinase to recombinant thrombolytic agents has been significant. Assuming there are

1.1 million myocardial infarctions per year in the United States and about 30 percent of these cases receive intravenous thrombolytics, shifting from streptokinase to t-PA (or a mutant of t-PA) adds about \$627 million to the national health budget solely for this aspect of caring for myocardial infarction.

IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICDs) CASE HISTORY

Mark Hlatky of Stanford University examined the early barriers to the development of ICDs. He said that the early ICDs were large, they could only give a shock, and they required open-heart surgery to be put in place. These initial technical limitations were at the beginning the major barrier to the use of ICDs. These limitations have now been largely overcome. The second early barrier was the high cost of both implanting and maintaining ICDs. This led to another major barrier, the lack of evidence of cost-effectiveness. The final early barrier was the need for specialized personnel to manage patients.

Regarding the determination of effectiveness, the RCT is regarded as the gold standard in the clinical community because it is the best way to ensure a fair comparison of two therapies. Further, the demonstration via an RCT that a therapy saves more lives is usually a tremendous marketing tool for the therapy.

Hlatky said that the ICD is an interesting case history for effectiveness studies. Ventricular fibrillation is fatal if not treated. So, it was argued that any time the ICD was activated a life had been saved. However, even though the ICDs were effective in converting ventricular fibrillation, many were skeptical that this meant the patients were actually living longer.

Eventually RCTs of ICDs were performed, but there were many problems. There was inadequate patient enrollment. Many physicians did not want to enroll patients into the studies because these physicians were convinced the device was beneficial. In addition, many patients did not want to be part of an experimental study. The second problem was what to compare the device against—no treatment or a drug treatment? The third problem was identifying who should be responsible for paying for the study—the National Institutes of Health, FDA, payers, or health care providers? The final problem was the generalizability of the trial findings. RCTs tend to be carried out in idealized circumstances in which patients are highly selected and the therapies are administered in the best clinical settings by the best personnel.

Hlatky said that there have been at least three major RCTs analyzing patients who had an episode of cardiac arrest or ventricular tachycardia. About 2,000 patients were randomized either to get an ICD or the best drug available. The results show that patients who were given an ICD had a 28

percent lower chance of dying of any cause and about a 50 percent lower chance of dying due to an arrhythmia (Connolly et al., 2000). Hlatky observed that this was considered convincing evidence that ICDs¹⁶ do enable people to live longer if they are chosen properly and have prior evidence of cardiac arrest.

INTRAVASCULAR ULTRASOUND (IVUS) CASE HISTORY

Elizabeth Nabel (NHLBI) considered the use of intravascular ultrasound (IVUS), a device inserted in blood vessels to acquire images using ultrasound technology. IVUS was first developed by academic cardiologists in the late 1980s. It was not FDA approved until the early 1990s. It has been used primarily as a diagnostic and research tool in many academic centers despite the fact that it has not been reimbursed for a number of years. Nabel argued IVUS illustrates that sometimes devices are developed but are not readily implemented, and their benefits may not be apparent for 10 to 15 years.

Nabel said that there are four different diagnostic uses for the device:

- to characterize the nature of atheromatous plaque;
- to detect plaque rupture;
- to detect transplant arteriopathy; and
- to ensure apposition in stent placements.

One of the major impediments to broad deployment of IVUS has been cost-effectiveness data. A study (Berry et al., 2000), carried out by the National Health Service R&D Health Technology Assessment Programme in Britain found that if IVUS were used at the time of angioplasty by traditional methods using balloon catheter or by stent deployment, the restenosis rate was approximately 16 percent. Without IVUS use, the restenosis rate was approximately 24 percent. The cost per restenosis event avoided was about £1,500 (\$2,200). After extrapolation to long-term outcome, the calculated cost per quality adjusted life-year was approximately £6,500 (\$10,000). The baseline quality gain was 0.03 years. These investigators argued that in terms of cost-effectiveness, the widespread use of IVUS was not worth the investment.

Nabel concluded that IVUS is a valuable clinical adjunct to angiography. It is estimated that 5 to 8 percent of all stents that are deployed use IVUS, and a number of clinical studies have shown that IVUS-derived

¹⁶The results of the MADIT II trial, announced after the conference, broaden the range of patients for whom ICD therapy is appropriate.

residual plaque burden is the most useful predictor of outcome following clinical interventions. Technical development has persisted despite the slow schedule of reimbursement. Major clinical applications were not anticipated at the time of initial development. Cost-effectiveness is unlikely to be demonstrated unless this diagnostic device is incorporated into a therapeutic device. In summing up, Nabel said that IVUS is an example where cost-effectiveness data showed that broad use in angioplasty was not justified, and, as a result, development of the technology has been slowed.

MEDICAL USAGE OFTEN PRECEDES EFFICACY ASSESSMENT

Robert Young of the Fox Chase Cancer Center pointed to the frequent occurrence of therapies that are widely used but poorly assessed for cost-effectiveness by referring to some of the tools for diagnosis of melanoma. He said that increasingly complex diagnostic technologies are emerging, ranging from photography, through digital imaging and epiluminescence microscopy, to qualitative image analysis. The last three are expensive and have been heavily promoted but poorly assessed for cost-effectiveness. Other widely used but poorly assessed therapies include maternal-fetal monitoring, bone marrow transplant in breast cancer, lung reduction therapy in emphysema, and Ca-125 and trans-vaginal ultrasound in ovarian cancer.

Young then outlined a number of reasons why this happens. First, payers (insurers, employers, HMOs, and CMS) have generally been passive about the need for objective assessment (via RCTs) of unproven technology. They have too often abandoned the design of clinical trials to whomever wants to do trials funded in whatever way they want to do it. As a result, the large amounts of incomplete but positive data generated result in the stimulation of public demand. Second, and perhaps equally important, physicians and patients in the United States are aggressive and interventionist about care. At the same time there is little congressional desire to control access to or utilization of new technology and courts tend not to side against the patient-doctor relationship.

Determining at the margin what medical innovation is worthwhile and what is not represents a major challenge. As Paul Citron of Medtronic pointed out, early cost-effectiveness studies for implanted devices are likely to present worst-case scenarios and could cause therapies to be abandoned prematurely. As a result there is a reluctance to pay for outcome analysis/cost-effectiveness studies. Young expressed the view that payers ought to take a more active role in trial design and fund the key trials. They should pay for the care and experimental costs *only* in the context of properly designed clinical trials and they should fund several sites for confirmation and comparisons.

Sean Tunis of CMS agreed with Young that payers should take a

greater role in clinical research. He said that payers and purchasers of health care need to know the clinical effectiveness of new medical technologies and, as a consequence, these stakeholders have a responsibility to participate in the clinical research process. Tunis said that Medicare had taken an important step in this direction by paying for the routine costs of care in federally funded or approved clinical trials following a recommendation made by an Institute of Medicine committee. Medicare is currently paying for the cost of experimental interventions in two clinical trials. One trial is evaluating lung volume reduction surgery and the other carotid stenting.

EVALUATION CHALLENGES FACING METASTATIC MELANOMA AND OTHER CANCERS

As background to his presentation, Richard Pazdur of the FDA described the basis for New Drug Application (NDA) approval. It is necessary, first, to demonstrate efficacy with acceptable safety through adequate and well-controlled studies and, second, to generate product labeling that defines an appropriate patient population and provides adequate safety information. In recent years the FDA has developed initiatives (for example, accelerated approval, fast track, priority review) to bring drugs to the market earlier in the approval cycle.

Turning to the regulatory challenges posed by metastatic melanoma, Pazdur said that the disease is characterized by a high degree of biological heterogeneity. Survival may be influenced by prognostic factors, and therefore it is important for clinical trials to be well balanced with regard to these factors. The advent of biological therapies has led to the approval of Interleukin-2. The delivery of high dosage Interleukin-2 usually requires intensive medical support with stringent eligibility criteria for inclusion in trials, raising the question of selection bias.

With respect to future regulatory challenges for oncology in general, Pazdur said that targeted therapies may make drug regulation easier. Treatment effects on better-defined populations are likely to be greater, requiring smaller clinical trials. Targeted therapies may also provide opportunities to look at novel surrogate end-points. This challenges both the regulatory and scientific communities to demonstrate that improvements in surrogate measures translate into improved clinical outcomes.¹⁷

¹⁷Two recent publications have addressed the complex issue of surrogate endpoints—Downing, Gregory J. 2000. Biomarkers and surrogate endpoints: clinical research and applications: proceedings of the NIH-FDA conference held on April 15-16, 1999, in Bethesda, Maryland. Elsevier, New York, NY, and Victor G. De Gruttola et al., 2001, Considerations in the Evaluation of Surrogate Endpoints in Clinical Trials. Summary of National Institutes of Health Workshop. *Controlled Clinical Trials*. 22(5):485-502.

There are other challenges. With the explosion of new agents that are being developed for medical oncology, the industry must identify those agents that are really important since it will not be possible to carry out clinical trials for every promising compound that is discovered. Pazdur pointed out that it is estimated that less than 5 percent of eligible patients are actually enrolled in clinical trials. He concluded by saying that efforts have to be made to increase enrollment in clinical trials.

CONSUMER GROUPS CAN HELP FOSTER INNOVATION

Fran Visco of the National Breast Cancer Coalition said that the NBCC stresses the importance of educating consumers on what is quality care and how they should go about getting it. The organization has developed a quality care guide that gives consumers a set of core values and an understanding of evidence-based decision making. The guide does not attempt to tell consumers what choices to make.

The NBCC has also been active in fostering clinical trials. It was a strong advocate of the Rockefeller-Mack legislation to provide Medicare coverage of routine patient care costs in clinical trials and helped bring about President Clinton's Executive Order mandating this coverage. The NBCC has also been active in getting the CMS to implement this legislation. At the time of the conference, however, Medicare had covered the routine patient costs of only two trials. One barrier for patients wanting to enroll in clinical trials is not knowing that they are taking place. As a result of initiatives by the NBCC and others, Section 113 of the FDA Modernization Act required the institution of a clinical trials data bank. The National Library of Medicine has set up the data bank but unfortunately the industry has not yet agreed to put their trials in the data bank. The Act does not provide any enforcement mechanisms.

The NBCC also favors direct consumer involvement in clinical trials to bring forward innovation, something recently endorsed by the *Lancet* (*Lancet*, 2001). An example of this is the Genentech-NBCC collaboration on the herceptin trial. NBCC participated in the trial steering committee, had representatives on the data safety monitoring board, and helped prepare the outreach materials. Genentech has publicly stated that as a result of the consumer collaboration herceptin was on the market two years sooner than otherwise would have been the case.

ROUTES FOR NEW TECHNOLOGY INTO THE MEDICARE PROGRAM

Sean Tunis explained that there are three main routes whereby new technology enters the Medicare program. One way is through the diagno-

sis-related group (DRG) for inpatient care and ambulatory payment classification (APC) system for outpatient care. If there exists a DRG/APC payment category for a particular condition new technologies can be added to the Medicare program by being billed under the existing DRG/APC for the condition. The second main route for new technology to enter the Medicare program is through the Local Medical Review Policy (LMRP) process. Individual insurance companies that pay medical claims at the local level have their own technology policies. These local insurance companies make most new technology coverage policy. The national level, the third main route, handles only a minority of coverage decisions, for example, where the new technology represents a significant medical advance or there are inconsistent local coverage policies.

Tunis said that over the last decade or two the national coverage process has drawn criticism for the length of time that it has taken to make coverage decisions and the lack of transparency of the process. In response to these criticisms CMS has made the following changes since 1999 (Tunis and Kang, 2001):

- A Federal Register notice described how the coverage process works and the timelines for this process.
- Every coverage decision is now accompanied by a memorandum posted on the world wide web explaining the rationale for the decision.
- The establishment of the Medicare Coverage Advisory Committee created a public venue for dealing with both general and specific technology issues.
- An evidence-based framework has been adopted for coverage decisions.

DEVELOPING A MORE SEAMLESS APPROVAL AND COVERAGE PROCESS

In his keynote address, Mark McClellan spoke about an initiative to create a more seamless approval and coverage process. The NCI, CMS, and FDA are jointly developing an integrated process which involves all parties getting together early in the process, for example, when a clinical trial is being designed. Through this process the manufacturer of the device/drug learns at an early stage the information requirements not just for the FDA's safety and efficacy evaluation but also for the CMS and private insurers' coverage decision process. This initiative currently includes technologies involved with imaging procedures in cancer and is organized through the Interagency Council on Biomedical Imaging in Oncology.

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Barriers to Medical Innovation

The Conference also addressed the drivers of medical innovation and, at much greater length during several panels, the barriers to medical innovation.

Key drivers of innovation were considered to be:

- a high level of public interest in health care issues;
- strong public support for increasing NIH research funds;
- substantial and increasing private investment in medical R&D, although private sector interest waxes and wanes depending on the attractiveness of other investment opportunities;
- the aging population—a side effect of better health—moving the focus to other diseases (e.g. Alzheimer’s disease); and
- public expectations in the United States that patients should receive the best quality science.

The conference discussed several barriers to medical innovation. These have been clustered under three headings—technical-level barriers, public policy barriers, and high-level political/economic barriers.

TECHNICAL-LEVEL BARRIERS

Regarding barriers to innovation, the focus of the conference was public policy and broader political barriers. Nevertheless, conference speakers

mentioned a number of technical barriers—two of these related specifically to cancer therapy and two were of a more general nature.

Inadequate understanding of the biology of cancer. Bruce Scharschmidt of Chiron made the point that through genome sequencing we have an abundance of targets. The key issue now is gaining a better understanding of the corresponding biology of these targets. We also need better information management techniques to handle data.

*Poorly predictive pre-clinical models for cancer therapies.*¹⁸ Scharschmidt also said that there are good animal models for developing drugs for Type 2 diabetes, but the same does not pertain to cancer products. Given the more sophisticated understanding of the molecular basis of cancer, there is not a comparatively sophisticated set of pre-clinical models. This is an opportunity for research investment.

Inadequate effort devoted to effectiveness analysis. Scharschmidt observed that cost-effectiveness is generally not rigorously assessed during the course of development. Drug and device development is an expensive and lengthy process. It is hard for companies to justify further dollars and time in cost-effectiveness studies, particularly as there are no agreed-upon set of measures by the industry and payers. As result, there is an opportunity to develop a stronger and commonly agreed upon scientific foundation for cost-effectiveness measures and studies.

Not enough patients entering RCTs (randomized controlled trials). Bruce Hillner of the Medical College of Virginia said that cancer patients are less likely than cardiovascular patients to be enrolled in RCTs. He identified several reasons for this. Patients are reluctant to accept the default arm of trials, often not considered an equivalent therapy. For many patients with cancer, treatment is a “one-shot chance” and they want to take the option recommended by their physicians. Further there is less reliance on evidence-based medicine in cancer treatment and too great a tendency for premature adoption of therapies based on presentations at major conferences. Finally, managed care plans generally refuse to encourage participation in trials.

PUBLIC POLICY BARRIERS

Reimbursement policies not friendly to innovation. David Lawrence reported on how the IOM Roundtable on Health Care Quality (Chassin et al., 1998) documented three types of quality problems—underuse, overuse,

¹⁸It should be noted that many other major diseases, such as heart disease, stroke and depression, also have poor pre-clinical models.

and misuse. The underuse and overuse of medical technologies suggest that the right incentives may not be in place.

Both Lawrence and Laurel Sweeney of Philips Medical Systems pointed out that fee-for-service payment systems reward individual acts by individual people. They do not support very well integrated delivery capabilities increasingly necessary to treat a wide range of chronic conditions, such as congestive heart failure and diabetes. Sweeney reported, however, that there are some hopeful signs. The University of Maryland Medical Center is to carry out a study funded by CMS to test the cost-effectiveness of disease management services for congestive heart failure. The study will follow about six hundred patients. Half of the patients will receive traditional care focusing on the patient's medication compliance and self-reported vital signs monitoring. The remaining patients will be split between the two test groups. Patients in one group will receive ongoing home visits from a nurse who will monitor their diet/nutrition and medications as well as keep track of their weight and blood pressure. Patients in the other group will use Philips Medical Systems' in-home monitoring system to monitor their weight, blood pressure, and pulse, with the information being transmitted electronically to a computer in the doctor's office.

Mike Atkins of Beth Israel Deaconess Medical Center and Harvard Medical School reported that Medicare does not fully reimburse the costs of HD IL-2 (high dose Interleukin-2) for the treatment of metastatic melanoma. As a result hospitals are not offering this treatment for metastatic melanoma and research into using HD IL-2 to treat metastatic melanoma is being curtailed. Several hospitals are not providing HD IL-2 treatment for metastatic melanoma even for those who can afford to pay, out of concern for equity issues, raising an ethical question on the right to the access of care.

Scharschmidt pointed out that currently there is no Medicare coverage for self-administered or injectable products unless there is an intravenous equivalent.¹⁹ This results in the anomalous situation of having two cancer therapies, herceptin and tamoxifen, for example, which are treated quite differently. Herceptin, which has to be given by physician/provider by intravenous injection, is reimbursable, whereas, tamoxifen, which is a tablet, is not reimbursable. There are currently about 30 oral anti-cancer products that are not reimbursable.

Rapidity of technological change threatens the ability of federal agencies to cope. John Ford of the House Committee on Energy and Commerce

¹⁹Medicare is barred by statute from reimbursing for prescription drugs, a matter of current and prominent policy controversy before Congress.

minority staff emphasized the paradigm shift taking place in medical science/innovation. Investments in innovation are increasing—the budget of NIH is being doubled; and, in parallel, private sector R&D expenditures are increasing. Different types of innovation are occurring, for example, tissue engineering and genomics/proteomics. Further, individual elements of therapies are continually being improved requiring additional regulatory approval.

The implications of this are threefold. First, the flow of innovation is going to stress if not overwhelm the regulatory system. Second, the knowledge base of the regulatory agencies will need broadening. In particular, there is inadequate understanding among regulators of how multiple therapies are used in practice, leading to inappropriate regulatory practices for combination therapies. Third, new public policies may be needed to regulate highly targeted biologics with potentially different economic structures than those of standard drugs.

Ford said that a factor that could have an important bearing on the FDA's ability to cope is the future of user fees for New Drug Applications. When demand at the FDA for approval of new drugs increases, the extra fees allow more resources to be made available. The Prescription Drug User Fee Act (PDUFA) of 1992 provided the FDA with increasing levels of resources for the review of human drug applications. The original act expired September 30, 1997, but the FDA Modernization Act of 1997 amended and extended PDUFA through September 30, 2002. The post-September 2002 arrangements for paying for New Drug Applications are currently under discussion.

Regulations inhibit innovation and are costly to implement. Lawrence in his keynote speech referred to excessive regulation of the health care industry. For example, CMS has 130,000 pages of rules, regulations, and guidelines whereas the IRS has only 10,000 pages. Kaiser Permanente did some very preliminary estimates of what it cost the HMO to deal with local, state, and national regulations in health care, and found that somewhere between 5 and 7.5 percent of the total annual revenue stream is devoted to meeting regulatory requirements. For Kaiser Permanente, that is a regulatory burden of close to a billion dollars each year.

Laurel Sweeney of Philips Medical Systems spoke about problems that might arise with the Health Insurance Portability and Accountability Act (HIPAA) of 1996 and the ensuing privacy standards released in April 2001. HIPAA's privacy regulations pre-empt any state from enacting laws that are contrary to the Act. However, the privacy regulations do not prevent states from enacting more stringent requirements, which some states are already doing. Sweeney believed that the end result would be a patchwork of state

laws, which could, in some cases, affect the ability to conduct clinical trials, resulting in a negative impact on innovation.

Public policy changes a major uncertainty for venture capitalists. With regard to investing in medical innovation, Brandon Hull of Cardinal Partners said that although venture capitalists understand how to evaluate technology and development risks, it is difficult for them to assess the degree to which the public policy rules will change. Hull said that to foster innovation public policies must be consistent in order to have a salutary effect on prices, the investments required, and the timeframe from idea to marketplace. He asserted that price controls are disincentives to investment and speculated that a mandatory pharmacy benefit under Medicare would likely be accompanied by price controls and therefore could be a disincentive to investment and innovation. Shortening the life of patents is also a disincentive to investment. In addition, a consistent approach to coverage and reimbursement decisions is desirable.

In recent years investment costs have been increasing. It has been 10 years since the discovery of the cystic fibrosis gene and there is still no therapy derived from this discovery. The timeframes and the amounts of money needed to develop genomic therapies are still unknown. The requirements for clinical trials and regulatory review are important determinants of overall development timescales—up to 8 years out of a typical 15-year development cycle for a new drug. Hull said that recent public policy changes have helped with carrying out clinical trials, and over the past few years the time for regulatory review has also improved.

Older public policies perhaps no longer providing the right incentives. Susan Foote of the University of Minnesota commented that over the years Congress has been very active in establishing medical technology policy. Major initiatives in the 1990s included the establishment of the National Institute of Bioimaging and Bioengineering (1993–2000), the FDA Modernization Act of 1997, Biomaterials reform in 1996, ongoing Medicare coverage and coding reform and conversion of the Agency for Health Care Policy and Research (AHCPR) into the Agency for Healthcare Research and Quality (AHRQ). Sweeney alluded to the more recent Balanced Budget Refinement Act of 1999, which enacted fundamental reform of the hospital outpatient payment system including the transitional pass through for medical technologies. This was followed a year later by the Benefits Improvement and Protection Act which extended the pass through to hospital inpatient technologies.

Against this background of legislation and in the light of the accelerated pace and the broadening scope of medical innovation, Ford thought it might be appropriate to review some older elements of medical technology policy, specifically the Bayh-Dole Act of 1980, the Orphan Drug Act of 1983, and the Waxman-Hatch Act of 1984, to see whether these laws are

still achieving their desired public policy goals. Both the Orphan Drug Act and the Waxman-Hatch Act were enacted in the early days of the biotechnology industry, and Ford questioned whether the incentives written into these two laws were still economically relevant.

Policies for managing conflicts of interest may end up inhibiting innovation. Tom Fogarty of Stanford University suggested that too many rules devoted to managing conflicts of interest in the care giving setting at the interface of the patient's needs and research objectives, may end up inhibiting innovation.²⁰ He observed that academics and clinicians have quite different objectives with regard to innovation. Academics' interests are focused on exploring new theories and carrying out experiments in laboratories while clinicians' interests are focused on using science for clinical purposes and assessing clinical utility. Against this background, he said concerns about conflicts of interest had become pervasive, particularly in academic medical centers. Patients want to go to the physician who is utilizing the best technology to treat their disease. That physician is most likely involved in innovation, and as such, is often prevented from treating the patient because of the "perception" of monetary gain through the physician's work in an innovative area. In such circumstances, Fogarty believes that the physician's interest in providing the "best" treatment for his/her patient is considered suspect, when in fact his or her actions are predicated on treating the patient with technology that is in "the patient's best interest." In Fogarty's view such conflicts of interest "are inherent to our very existence and represent a critical element in all relationships." Attempts to legislate honesty and integrity or lack thereof will not work. Honesty and integrity should certainly be monitored, albeit at the local level.

HIGH-LEVEL POLITICAL/ECONOMIC BARRIERS

Congressional reluctance to address health care issues. Congressional reluctance to address health care issues is understandable given the highly technical nature and complexity of the issues and the fact that legislators and their staffs often lack the knowledge base to fully address the issues. Further, it is increasingly difficult for politicians to benefit from engaging

²⁰Since the conference the AAMC has produced guidelines on the oversight of individual financial interest in human subjects research (Protecting Subjects, Preserving Trust, Promoting Progress. Task Force on Financial Conflicts of Interest in Clinical Research, AAMC, December 2001) and the GAO has reported that academic medical centers are not doing enough to identify and deal with conflicts of interest (Biomedical Research: HHS Direction Needed to Address Financial Conflicts of Interest. GAO-02-89, November 2001).

health care issues. Jamie Robinson of the University of California at Berkeley pointed out that government, like all the other stakeholders in the health care industry, is totally disenchanted with managed care (Robinson, 2001). He believed the key lesson of the 1990s for government, as for the other stakeholders, is not to get between the consumer and what the consumer wants to consume. Political capital cannot be gained by attempting to allocate scarce health care resources. From an electoral perspective it is better for politicians to criticize the industry from the periphery.

Responding to Lawrence's comments about fragmentation on the health care delivery side, Susan Foote said that the political side was also fragmented. Institutional changes had occurred internally in Congress, and entrepreneurial politics had got in the way of developing comprehensive solutions to health care problems. Foote pointed out that this fragmentation is compounded by the piecemeal nature of medical technology policy. Despite the pervasiveness of medical technology policy, each major piece of legislation is responsive to different social and political pressures. Moreover, legislative responsibilities of the various House and Senate committees are jealously guarded in Congress. Sometimes these policies conflict, as for example, in the case of safety. The FDA defines product safety criteria, while in product liability legislation there are other definitions of product safety that emerge from court decisions at the state level.

Increasing scrutiny of prices could influence return on capital. Robinson pointed out that all stakeholders have become disenchanted with managed care and are increasingly reluctant to make choices on behalf of consumers/patients. So, by default, consumers have to make more of the choices (Robinson, 2001). As part of this move toward consumerism, employers have followed the pensions model and shifted from defined-benefit models to defined-contribution models for health care benefits. Employees will be offered a range of packages of health care benefits at different price points. At the same time consumers will be faced with higher deductibles and co-payments.

An important consequence of the trend toward consumerism in health care will be increased consumer scrutiny of costs. The American consumer values new medical technology, strongly supporting public investment in NIH research, for example, but is less enthusiastic about paying for high up-front R&D costs for medical products. Consumer concerns about costs could threaten the return on innovation through the emergence of differen-

²¹A full discussion of equity issues as they relate to health care was beyond the scope of the conference. The Institute of Medicine's Committee on the Consequences of Uninsurance is studying uninsured Americans in a series of six reports over the next two years, beginning with the recently published report *Coverage Matters: Insurance and Health Care*.

tial pricing models, political pressure to cut costs, and pressure to shorten patent lives.

*Lack of responsiveness to equity issues.*²¹ Ford said that basic public support for federal funding of medical research programs rests to a certain extent on equitable access to the fruits of the research. Political support for high levels of NIH funding could be undermined by an increasing proportion of the population lacking health insurance or by the continued absence of a prescription drug benefit under Medicare.

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Appendixes

A

Conference Agenda

The National Academies
Board on Science, Technology, and Economic Policy
Board on Health Care Services, Institute of Medicine

Agenda

Conference on
Medical Innovation in the Changing Healthcare Marketplace

June 14-15, 2001

National Academies Main Building
2100 C Street, NW, Washington, DC

June 14

8:00 AM Continental Breakfast

8:30 AM *Welcome and Introduction of Keynote Speaker*

Cochair: Ed Penhoet, UC Berkeley

8:35 AM *Keynote Address—Encouraging High-Value Innovation:
Medicare and Other Federal Policies*

Speaker: Mark McClellan, Council of Economic Advisers

9:15 AM *Objectives for the Conference*

Cochairs: Ed Penhoet, UC Berkeley, and Kathy Behrens,
RS Investments

The cochairs will outline the background to and their goals for the conference.

9:45 AM *Report from an NAE Workshop on Engineering and Health Care Delivery Systems*

Speaker: **Jerry Grossman**, Kennedy School of Government,
Harvard University

10:00 AM *Panel I: The Macro Picture—Trends in Health Care Costs and Benefits*

This session will examine at the macro level the extent to which new medical technology is driving up health care costs and, the equally important issue of whether new medical technology is bringing more benefits.

Moderator: **Philip Aspden**, NRC

Panelists:

- **Sheila Smith**, CMS, formerly HCFA
- **Alison Keith**, Pfizer, Inc. (ret.)
- **Kevin Murphy**, University of Chicago

11:15 AM Break.

11:30 AM *Panel IIA: Cardiovascular Disease—Trends in Health Care Costs and Benefits*

In this session the panelists will examine in more detail trends in the costs and benefits of new medical technology by considering cardiovascular disease. The long-term health care cost implications of successful treatment of cardiovascular disease will be considered.

Moderator: **David Gollaher**, California Healthcare Institute

Panelists:

- **Elizabeth Nabel**, NHLBI
- **Dan Mark**, Duke University
- **Paul Citron**, Medtronic
- **David Cutler**, Harvard University

1:00 PM Lunch

2:00 PM *Panel IIB: Cardiovascular Disease—Fostering High-Value Medical Innovation*

Panelists will examine the barriers to innovation in the development, adoption, and diffusion of new treatments of cardiovascular disease. Ways to overcome identified barriers will also be considered.

Moderator: **Kathy Behrens**, RS Investments

Panelists:

- **Tom Fogarty**, Stanford University
- **Mark Hlatky**, Stanford University
- **Laurel Sweeney**, Philips Medical Systems

3:30 PM Break.

3:45 PM *Panel IIIA: Metastatic Melanoma—Trends in Health Care Costs and Benefits*

In this session the panelists will examine in more detail trends in the costs and benefits of new medical technology by considering metastatic melanoma. The long-term health care cost implications of successful treatment of metastatic melanoma will be considered.

Moderator: **Gil Omenn**, University of Michigan

Panelists:

- **Steven Rosenberg**, National Cancer Institute
- **Mike Atkins**, Beth Israel Deaconess Medical Center, Harvard Medical School
- **Margaret Tucker**, National Cancer Institute
- **Bruce Hillner**, Medical College of Virginia

5:30 PM Close

6:00 PM Reception

* * * *

June 15

8:00 AM Continental Breakfast.

8:30 AM *Welcome and Recap*

Cochairs: **Ed Penhoet**, UC Berkeley, and **Kathy Behrens**, RS Investments

8:45 AM *Key Note Speaker*

Speaker: **David Lawrence**, Kaiser Permanente

Dr. Lawrence will speak about the recent IOM report, *Crossing the Quality Chasm*, medical care in the 21st century, the drivers of innovation, and possible public policy levers to foster high-value medical innovation.

9:45 AM *Panel IIIB: Metastatic Melanoma—Fostering High-Value Medical Innovation*

Panelists will examine the barriers to innovation in the development, adoption, and diffusion of new treatments of metastatic melanoma. Ways to overcome identified barriers will also be considered.

Moderator: **Ed Penhoet**, UC Berkeley

Panelists:

- **Bruce Scharschmidt**, Chiron
- **Richard Pazdur**, FDA
- **Robert Young**, Fox Chase Cancer Center
- **Jonathan Lewis**, Antigenics

11:00 AM Break.

11:15 AM *Panel IV: The Macro Picture—Fostering High-Value Medical Innovation*

In this session panelists will examine public policy initiatives at the macro level that will foster the development, adoption, and diffusion of high-value medical innovation.

Moderator: **Alan Garber**, Stanford University

Panelists:

- **Susan Bartlett Foote**, University of Minnesota
- **Sean Tunis**, CMS, formerly HCFA
- **Jamie Robinson**, UC Berkeley

1:00 PM Lunch

1:30 PM *Panel IV (cont.): The Macro Picture—Fostering High-Value Medical Innovation*

Panelists:

- **Brandon Hull**, Cardinal Partners
- **Fran Visco**, National Breast Cancer Coalition
- **John Ford**, House Committee on Energy and Commerce/
Democratic Staff

2:45 PM *Session VI: Wrap-up Discussion*

The final session will allow participants to discuss the key issues arising from the conference.

Moderators: Cochair: **Ed Penhoet**, UC Berkeley, **Kathy Behrens**,
RS Investments.

B

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C
Keynote Speech:
Encouraging High-Value
Medical Innovation

Mark McClellan, Council of Economic Advisers

MEDICAL INNOVATION AT POLICY CROSSROADS

I have been nominated for the Council of Economic Advisers²² to coordinate economic issues in health care policy for the Bush Administration. The topic of medical innovation policy is an area of major interest and importance to the Administration. The President in his campaign emphasized the need for better mechanisms for assuring that people get access to valuable new medical technologies and continuing to improve access to existing technologies. It is very clear from research done by participants in this conference that medical technology has contributed enormously to the improvements we have seen in health in this country in recent years, especially improvements in the length of life and the quality of life for older Americans.

Medical innovation has also become a major part of U.S. economic growth. For example, in the last several years as investment in some of the Internet technologies has slowed down, there has been a continuing explosion in investment in biotechnology products. I think that is one of the major areas of venture capital investment today, which harbingers well for the future of this part of our economy in terms of continuing to contribute to economic growth.

Obviously an administration's policy should be to encourage more of

²²Mark McClellan was confirmed by the Senate on July 25, 2001.

this valuable medical innovation, but medical innovation has also been marked by rapid increases in health care costs. I do not need to tell you that changes in medical treatments, not rising prices or other factors, have been the major cause, at least up until now, of some of the increases in health care costs in this country, particularly Medicare costs.

So, we are at a policy crossroads. On the one hand we face very strong pressure to try to encourage innovation. On the other hand there are growing concerns about the fiscal and economic implications of the costs of medical innovation. This comes to the fore in the Medicare program. On the one hand, we are strongly advocating mechanisms that would help seniors get valuable new technology sooner. On the other hand we are equally strongly trying to make a case for the need for careful fiscal planning and economically sensible policies because of concerns about the long-run fiscal status of Medicare.

ENCOURAGING HIGH-VALUE MEDICAL INNOVATION

This comes down to the critical question of how do we encourage high-value medical innovation? Not just innovation involving new technologies that may or may not have an impact on actual health outcomes, but how do we encourage more technologies that really are worth the cost? Ideally some of those would end up saving money as well. Again, we have not seen a tremendous amount of that in recent years. Perhaps through better policy making we could encourage more innovation that leads to lower health care costs as well as improved health. In terms of the incentives for innovation that policy might influence there are three major areas. I would like to hear what your views are on this, and whether there is an area that we are leaving out or not supporting properly.

Support for Biomedical Research

What many people focus on first when they think of innovation is support for biomedical research and fundamental research. This is an area where federal policy has seen a big infusion of dollars in recent years. The President just like the previous Administration has committed to a doubling of the NIH budget between 1995 and 2003. I think the original goal was to do it in a decade. According to our budget resolution, it will be done in just 8 years. So, at least in the biomedical community there has been a huge infusion of federal research dollars and that is going to continue over the next several years. Getting good products and valuable innovations into use requires more than direct federal support for medical innovation research, however.

Coverage Decisions

A second part of the innovation process is coverage decisions. Once medical technology has been developed, what steps are needed to ensure insurance coverage and adoption in medical practice? In this area there have been concerns raised about delays. Partly this comes in the area of the FDA approval processes and the multiple steps required to bring a drug to market. Beyond that there are coverage decisions by the Center for Medicare and Medicaid Services (CMS, formerly the Health Care Financing Administration), and other payers.

The most interesting recent developments that we have been considering for application elsewhere have come from collaborative projects started by Richard Klausner at the National Cancer Institute between the NCI, the FDA, and CMS. This process currently involves primarily those technologies involved with imaging procedures in cancer and collaboration between all of the parties that need to reach agreement on the evidence available to bring a new product to market. This collaboration involves individuals from NCI, from CMS, and from FDA sitting down early in the innovation process, typically when a clinical trial is being designed. In one integrated process the drug or device manufacturer can pull together all of the evidence that is needed, not just for the FDA's safety and efficacy evaluation but also for the coverage process which takes place at CMS and other private insurance companies. The information required for these different processes is somewhat different and historically the process has been much more of a sequential one. The clinical trial is first and that leads to a conclusion about the safety and efficacy of the treatment. Then further studies are carried out on costs and other issues that need to be addressed for coverage decisions.

Having an integrated process that brings all the parties together early on while a clinical trial is being designed can potentially speed up the process for moving valuable new technology into active practice by some years. This model may be applicable to other areas. It seems to me that it holds a lot of promise.

Diffusion of New Technologies

The coverage decision process is an important part of bringing innovations to market and into actual medical practice, but beyond that there is a third area that does not get enough attention in studies of medical innovation. This area is the process by which new technologies diffuse into widespread practice. There have been some studies by a number of reputable experts on issues related to evidence-based medicine that show that some

medical technologies can take as long as 15 or 20 years to fully reach widespread adoption in medical practice.

In addition, studies show that many medical technologies are being used inappropriately. These technologies are widely used in some parts of the country and in some institutions. These variations seem much larger than can be explained for economic or clinical reasons, even though they may, in part, be due to differences in the preferences in the community and to differences in the skills of physicians and other health care providers in the community. It is these kinds of variations that account for much of the potential for improving the value of medical innovation in practice.

Some of you may have seen Secretary O'Neill's testimony with the release of the Social Security and Medicare Trustees' Annual Report in March. He talked about the potential for substantial savings from improving the way that medical care is delivered, for example, taking more steps at the local practice level to identify ways to deliver more cost-effective care.

He spoke of applying what he called the "Toyota" principles of management, whereby everybody involved in a complex organization like a hospital has the opportunity to think about the specific things that they can do to improve the quality and reduce the rate of errors in the services that they deliver. These are typically not very high-tech things, for example, ensuring that errors in transcribing of medications do not occur. They can lead to substantial savings and, at a minimum, substantially higher value in the delivery of care provided. This also extends to the use of medical technologies for indications that may not be very well justified or there may be evidence that the technologies are not being used appropriately. Yet, they still find their way into active practice. If there were some federal levers that we could use to help bring better practices into being, we could avoid delays in appropriate use of medical technologies, and move away from inefficient and wasteful styles of medical practice.

This is a very hard thing to do. As you all know, patients are different in important respects, and there are many patient preference factors and clinical factors that go into most medical decisions. Moreover, it is not something that is very easy to legislate or to regulate centrally. To move forward on this issue we have thought about whether there are ways to provide better incentives to organizations, to health plans, and to providers.

As Secretary O'Neill and Secretary Thompson have noted, it does not seem to make much sense in Medicare to pay more to hospitals that are delivering bypass surgery operations that result in complications and re-admissions than to hospitals that can deliver a low complication rate surgical procedure with fewer re-admissions. This is a difficult area to make progress in because of the complexities of our current fee-for-service payment systems, and I do not want to make this sound like private insurance plans have all the solutions here either.

A big problem with capitated payments or payments that move away from paying on a fee-for-service basis is that they may not provide appropriate incentives to deliver costly care when it is truly valuable. We are struggling with ways to help policy move forward effectively. Once again some help from you on new directions for medical innovation policy would be very useful.

We look forward to the results of this conference and subsequent meetings of this National Academies working group with a lot of anticipation. We hope that they will lead to some ideas that we can translate into practice.

DISCUSSION

David Beier, Hogan & Hartson LLP: A question and an observation. As you think about the Human Genome Project being a merger of computer science and biology, increasingly you are going to have complicated problems if you only fund biomedical research and not the National Science Foundation and the other elements of the federal research portfolio. Could you comment on the President's budget in this respect?

One of the problems of collaboration among the FDA, the NIH, and CMS is that you run the risk of creating a third approval hurdle of cost effectiveness for products, and of having federal bureaucrats essentially make that decision rather than the market or the medical practitioners. I would like to get a comment about how you avoid doing that if you go down that collaborative route.

Mark McClellan: With respect to the importance of innovation in areas that might not be thought of as directly related to biomedical science, I looked back over some of the recent funding decisions by the NIH and was impressed to see how much of their work is in areas that I think most people would consider computer science. There are major investment programs related to super-computing technology and collaborative projects across institutions to do next generation computing and information storage. The NIH knows that the future of biomedical research depends critically on innovations in such underlying technologies as medical information systems.

We are undertaking a review of whether there are better ways to fund some National Science Foundation research as well as to make sure it is coordinated with the expanded research enterprise at NIH. It has been interesting, though, to see the level of political support for NIH research, far and above some of the other areas of basic research that are clearly related to NIH. I think basic research is something that we want to make sure continues and that integration between basic research and applications at NIH also continues.

With respect to whether what we intend to be a streamlining of the technology approval process may become another bureaucratic hurdle in an already time-consuming process, I think that is a risk. I am not sure that the model that Dr. Klausner has developed so effectively in one part of NCI is a universally applicable model, although it does have support from manufacturers and is widely regarded as having shaved substantial time off the approval process. This is the kind of issue on which we could use some expert guidance to make sure that we are really taking time out of the approval process rather than just creating additional hurdles. These are not easy questions, and that is why I am glad the National Academies are focusing on them.

Gil Omenn, University of Michigan: Your third challenge about how to get the right incentives is directly relevant to a new study launched in April with a meeting here at the Institute of Medicine. It will be the follow-on to the *To Err Is Human* report and the *Crossing the Quality Chasm* report.

The specific mandate from Congress is to look at the quality oversight and the quality improvement activities of federal agencies including the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), National Quality Forum (NQF) and other quality activities in the private sector and the not-for-profit sector. The present mandate, as interpreted by the IOM, excludes dealing with the reimbursement mechanism. In a few sentences, you made a powerful case that we need to find ways to tie the payment system together with incentives for support of what works and blocking things that do not—what is safe and what is not at the product level, the service level, and of course, the system level.

Mark McClellan: I think it is very important that reimbursement not be overlooked. It does have a big impact on medical practice and on the use of treatments. It is an area where bold thinking is needed. This is a controversial area. There are no obvious general solutions, but it is an area that we would like to incorporate in policy making, and so we look forward to any guidance you can provide.

Mary Jo Deering, Department of Health and Human Services: You observed that costly care is often valuable. You also noted that improvements in longevity are attributable to medical innovations. I think there is a large body of literature indicating that longevity is also due in part to public health and primary prevention efforts. Yet the percentage of health care expenditures devoted to prevention has been estimated to be as low as 1 percent and no higher than 5 percent. Is there anything that you see on the horizon that would help encourage innovation in less costly preventive interventions?

Mark McClellan: The question of innovation and less costly preventive treatments is a good one. It is related, in part, to the reimbursement

issue to the extent that providers and makers of medical technology and others involved in the health care system are paid more when they do more, paid more for complications, and paid more for treating the consequences of poor preventive care. It does not seem that the incentives are in the right place.

I noted you are from HHS and this is a concern that has made its way to the Secretary's level. I think you will see some more announcements and initiatives coming out of your department in the months ahead. These are aimed at helping prevention regain a central place in our provision of health care and taking steps to try to make it easier for people in public programs, as well as in other insurance programs, to get the preventive care they need and to help them know when they need it.

I did not mean to say that the use of medical technologies when diseases actually occur were the only, or even perhaps, the main contributor to improvements in health and the quality of life that we have seen in recent years. Prevention is obviously an important part, and I hope that your work here on medical innovation can help us find ways to better support innovation that is geared towards prevention as well as treatment.

Philip Aspden, NRC: We have got a question from a webcast listener, Curt Shoemaker of Johnson & Johnson, and his question is brief. How are new technologies and new procedures selected for the NCI/FDA/CMS collaborations that you mentioned earlier?

Mark McClellan: I think they have focused on imaging procedures because the coverage issues that needed to be addressed are relatively well defined. If, however, this turns into a large and complex procedure, it can end up being quite time consuming and may not help achieve the desired goal of reducing the time to market.

Dan Mark, Duke University: As a practicing clinician, I see one of the biggest impediments to improving the efficiency of our care and to addressing the concerns about medical errors to be the lack of an appropriate informational infrastructure—an electronic medical record that spans across the entire system and allows us to integrate information efficiently.

The marketplace has been unable to respond to the deficiency perhaps because IT suppliers see doctors are still using many techniques we used in the last 100 years or so. William Osler, if he were reincarnated, would probably still be comfortable with our medical records. They have changed very little. If the marketplace is going to be very slow in responding to this, I wonder whether there is a role for the federal government. Is there some way to accelerate this process? I do not see that there is going to be the technological infrastructure to support some of the initiatives that are being talked about to improve quality if the information systems cannot be brought up to speed.

Mark McClellan: It has been very difficult to develop good informa-

tion systems in health care in contrast to many other industries. I think there are several reasons for this. One of them may be privacy concerns. As you know, there has recently been a controversial series of policy developments related to privacy issues. We are trying to go forward establishing some uniform privacy standards as soon as practicable over the next couple of years in a way that is not overly burdensome for the health care industry to implement.

Another impediment may be that the financial rewards for good information systems are not comparable to those in other industries. It is interesting to contrast the health care industry and the financial services industry. Very sensitive information is involved in both cases but I think no one would have any concerns about an ATM transaction passing across a shared network. It is handled privately. It is handled without error. It is handled with consistent standards across the board. In health care, we do not have in place either the privacy standards or the data standards or the infrastructure itself.

In terms of standards, I think the federal government is trying to move forward as quickly as we can with developing Health Insurance Portability and Accountability Act (HIPAA) and other coding terminology standards, and the establishment of the computer and data infrastructure needed to share data effectively. Again, privacy protection is an important part of this.

I still wonder whether some of these investments in computer technology are really all that promising in terms of reducing errors or delivering higher quality care. We hear a lot from hospitals and other institutions that just say, "Look, this new computer technology requires a substantial investment, and we just do not have the funds to do it." I wonder if this is a function of reimbursement incentives that in many cases are not paying more and maybe even paying less to hospitals that deliver care without complications.

I hope that this or other groups can provide some guidance on how we can improve policies in this area. I know there are many proposals pending in Congress, ranging from grant programs to demonstration projects, to implement better computer systems. It is a critical part of health policy and innovation.

D

Keynote Speech: Bridging the Quality Chasm

David Lawrence, Kaiser Permanente

I am going to talk about the IOM report *Crossing the Quality Chasm* and I wish to address it from the perspective of trying to deal with the scientific and technological breakthroughs as they are made available to the health care delivery system. We struggle to keep up with the pace of innovation and to move these innovations into practice in a way that is safe, responsive, and high quality.

As Jerry Grossman pointed out yesterday, it is fair to say that “the tools of care” have far outstripped “the tools for caring.” The science and technology of medical care have moved far faster than the tools we have available for delivering these breakthroughs. Stated somewhat differently, over the last half of the 20th century we have tried in a variety of ways to attach a more and more sophisticated jet engine to a horse and buggy in order to make a jet airplane. We continue to struggle with what happens when we try to deliver highly sophisticated and increasingly complex science and technology through a system that is not up to the task.

THE IOM QUALITY OF HEALTH CARE INITIATIVE

Thinking about the subject of the IOM reports really began in about 1995 here at the IOM when we had a roundtable on quality of care, cochaired by Bob Galvin from Motorola and Mark Chassin, the then Commissioner of Health in New York, and now at Mount Sinai Hospital, New York. We looked at the whole question of what was happening with the quality of care in the United States. We looked at about 30 years worth of

documentation and identified conclusions that were summarized in a paper in the *Journal of the American Medical Association* in 1998.²³ Somewhat overstated, the quality of care in the United States approximates a random walk. The quality is highly variable. There is a substantial amount of overuse, misuse, and underuse of the available science and technologies—all independent of geography, independent of payment type, and independent of when or where people were trained to practice as physicians.

It was a rather devastating conclusion. From that roundtable, the IOM launched the next series of studies, overseen by the Committee on Quality of Health Care in America, chaired by Bill Richardson, formerly the president of Johns Hopkins University and now head of the Kellogg Foundation. Chuck Buck and I were on that committee, and several others participated, including Jerry Grossman. In the second piece of work that we did, we focused on the issue of safety. It led to the *To Err Is Human* report published in 1999. This spring, we published the final report *Crossing the Quality Chasm*.

THE SYMPTOMS OF A SYSTEM THAT IS BROKEN

The quality and safety reports are linked together. Essentially, the examination of quality and the examination of safety were both looking at the symptoms of a system that is broken. As we examined that system, we came to more and more firm conclusions that there was a mismatch between the rate and the quantity of scientific and technological innovation occurring and the ability of the delivery system to deliver it safely and responsibly. When we published the last report, it was an attempt to understand in more detail the nature of that mismatch and to recommend interventions that could accelerate the rate of innovation on the delivery side to improve the match between the care and the caring.

What I would like to do is briefly review those symptoms for you, talk about the reasons for the conclusions we reached in the IOM report, and then describe the opportunities for innovation on the delivery side. In so doing, I will touch briefly on some of the policy levers, because there are significant policy barriers or opportunities among the various tools that we have available for intervening.

Wide variations in quality practice were documented back as far as 1975 in the small area variation analysis by John Wennberg, MD, and in a variety of studies across the country over the last 30 years. The more recent

²³Chassin, Mark R., Robert W. Galvin, and the National Roundtable on Health Care Quality. 1998. The urgent need to improve health care quality. *JAMA* 280(11):1000-1005.

safety studies, primarily but not exclusively those of Lucien Leape and his colleagues at Harvard, identified occurrence of a variety of medical errors that result in morbidity and mortality—errors caused not by physician malfeasance, but by system error.

The numbers of hospital deaths range anywhere from 30,000 to 80,000. At this point, we have no understanding and little documentation of the rate of error that is occurring in the ambulatory setting. We have some early estimates from the *British Medical Journal* and others, some work in England, and some work in the United States. The total number of deaths occurring as a result of errors in the health care system we think could be as high as 150,000, or even 200,000 per year.

There is another measure that Barbara Starfield has published in a *JAMA* article a year ago. Dr. Starfield looked at the whole question of system-related deaths for whatever reasons, including errors. Her conclusion was that there are somewhere between 200,000 and 250,000 deaths per year from system-related causes, of which error is the most notable. Starfield also made interesting comparisons between our system and others, using a variety of measures of health outcomes. She concluded, as many have, that although we spend an enormous amount on health care and lead the world in scientific innovation and technology, the results in terms of improved health do not match that level of investment.

There are other symptoms that we looked at in the IOM study. One of them has to do with responsiveness. In the Picker Institute studies of patient assessment of their health care experiences, about three-quarters of those surveyed indicated that their experience with the health care system led them to conclude that it was a “nightmare” to navigate. They identified duplication, lack of communication, conflicting points of view about what should be done, and lack of understanding about what the science suggested. In summary, we have a non-patient-centric system. It is a system that is fragmented and fractured.

Finally, we examined data on the cost of poor quality care, which has interesting implications for innovation. Between 30 and 40 cents of every dollar spent on health care is spent on the costs of poor quality. This is an extraordinary number representing slightly more than about a half trillion dollars a year. That is a vast amount of money wasted on overuse, underuse, misuse, duplication, system failures, unnecessary repetition, the lack of communication, and inefficiency.

These high costs of poor quality are not much different from the experience that General Electric Co. and others have had in more tightly managed and highly organized manufacturing systems. When one seeks to understand what the costs of poor quality are, it is not unusual to find substantial opportunities for improvements in the cost performance of the system, by applying the tools of quality improvement. Health care does not

even come close to matching well-organized, systematically designed production or manufacturing systems.

Our experience in Kaiser Permanente suggests that these numbers are not exaggerations. When seeking opportunities to improve the organization and delivery of care, we often find substantial improvements in the underlying cost performance of the organization. In fact, the whole premise on which we compete is to drive costs down by improving quality.

TREMENDOUS GROWTH IN THE COMPLEXITY OF HEALTH CARE

Why is this happening? What seems to be the problem for health care here? There are five major issues that I want to highlight. The first is that most of the scientific and technological breakthroughs that have occurred since World War II have not simplified the task of taking care of patients. They have made it more complex, or certainly raised the standards for delivery of quality care. Here are a few examples, to make the point:

- At the end of World War II, as we entered the 1950s, there were about 10 to 12 categories of health care professionals in the United States. Today, there are over 220 categories of health care professionals.
- Right after World War II, there were about six to eight—depending on how you counted them—specialties in medicine. Today, there are over one hundred.
- In 1970 shortly after I finished medical school, there were approximately 100 published randomized control trials in the American medical literature. In 1999, there were just under 10,000 published that year alone. One-half of all of the randomized control trials published in the United States have appeared in the last 5 years.

Consider a disease like pediatric asthma, and look at what has happened since 1950 in the way in which we care for children with asthma. We have added an extraordinary array of drugs, an astonishing array of diagnostic instruments, and a considerable science concerning not only how to care for the individual with asthma but also how asthma is triggered. We also have a good understanding of how to educate families so that they can more effectively participate in the disease management process.

Science and technology have certainly stimulated a growing complexity in medicine. Increasing numbers of people involved, increasing categories of people involved, increasing expectations about what has to be done to treat people well, and increasing science and technology to manage in the process. Largely as a result of science and technology advances the medical care system is far more complex in terms of the number of institutions and

types of health care practitioners that are engaged in it than was the case in 1950.

MULTIPLE CONNECTION POINTS TO THE HEALTH CARE SYSTEM

As a result of this increased complexity, it has become much more difficult for the individual to connect with the medical care system, and patients and families have multiple connection points with the health care system. I often ask audiences to whom I speak, how many have a chronic illness or are taking care of someone with a chronic illness. Typically, about half the audience raise their hands. I then ask them how many people they connect with in the health care system. The first thing they do is count the doctors. It is anywhere from 3 to 10, depending on the nature of the illness. When I say, “What about the nurse, the pharmacist, the nutritionist, the physical therapist, and so on?” The numbers go up as high as 50 to 75 contacts.

That is issue number one. This is a system or non-system that has grown enormously over the last 50 years, and it has failed to keep the patient and the patient’s family at the center of its enterprise. It is small wonder that people identify the system as a nightmare to navigate. It is not patient-centered.

LACK OF ATTENTION TO PRODUCTION DESIGN

What would happen in sectors where the complexity of the system had significantly increased? You would create a highly sophisticated production design or manufacturing design process to handle the complexity. You would invest in an information technology infrastructure. You would create teams. You would create flow systems to manage the support activities required to carry out these processes. You would change the training of the people involved. You would work very hard to set new standards for what is quality in the production process.

In medicine, we have done very little of this. Physicians are still trained with the principle of individual, professional autonomy and yet, in reality they are not working in autonomous situations at all. Production design is a foreign word. In fact, it is almost sacrilegious to talk about production design in medicine. This is a religion we practice, not a science. This is not a production process that we are engaged in; it is an act that comes close to approximating what a priest does with a petitioner in a confessional box. We have not created the tools, the capabilities, or the mindset to respond to this complexity on the delivery system side. We have not applied the tools of production design at the units where patients get care.

DIFFICULT TO SCALE-UP HEALTH CARE DELIVERY

The third issue that we identified is that it has proven extraordinarily difficult to scale up medical care delivery. We have not been able to create very many examples of scaled delivery where the care is integrated across the ambulatory and inpatient settings and the other settings in which care is given such as the hospice or the home. We have not found very many systems that enable physicians to work in collectives. We have not found many systems that enable us to capture capital and re-invest capital in the delivery system infrastructure. With 80 percent of physicians in groups of less than 10, we still operate as though medicine were a single interaction between a patient and a doctor. While the patient-doctor interaction remains absolutely essential to the enterprise, the enterprise itself now involves a much more complex set of interactions.

Apart from the Veterans Health Administration, Kaiser Permanente is the largest delivery system operating at any scale, with 10,000 physicians. The next largest may be the Mayo Clinic. Most of those that remain are regional players on the delivery system side. We have scaled up enterprises on the insurance side but not on the delivery system side. Until we understand how to make that happen, it will be difficult to collect and reinvest the capital required to build and support the production capability essential to deliver the science and technology that the innovators are creating for us.

A PUBLIC POLICY ENVIRONMENT INHIBITING THE RESHAPING OF THE DELIVERY SYSTEM

Fourth, our public policy environment is structured to inhibit the reshaping of the medical care delivery system. Let me give you a couple of examples. In Wisconsin, there are 27 licensed categories of health care professionals, each with its own board of practice. Medicine is about removing boundaries so that people can flow seamlessly among a variety of practitioners, based on what the technology requires and what the patient needs. These regulatory or license-based silos create barriers between one professional and the next. You have to break through these barriers to create teams and to deliver the integrated care. It can be done, but with great effort. The licensing system is designed to protect the interests of particular professional groups within medicine, not to enhance the creation of integrated delivery capabilities.

Another example is the staffing requirements built into law. I sit on a board of Agilent Technologies, a spin-off of Hewlett-Packard. Imagine what would happen if there were a legal requirement that on the production line at Agilent a certain number of people of a certain kind of training had to operate and work for a certain number of hours. Agilent would go

up in smoke. Silicon Valley would go up in smoke for reasons other than economic downturn. Of course it would not happen. Any legislature that tried to pass that would be impeached.

In health care, we wrestle constantly with efforts to freeze the system in the name of patient safety and quality of care by mandating staffing requirements. When you think about health care as a process that has to innovate in its “manufacturing” as rapidly as it is innovating in its “products,” freezing the delivery system by laying out the staffing requirements is a remarkably stupid thing to do. Yet, we continue to do it, state by state.

Let us take another example. CMS, formerly HCFA, has 130,000 pages of rules, regulations, and guidelines that we have to deal with, while the IRS has only 10,000 pages. This suggests that there may be excessive regulatory costs that inhibit building the IT infrastructure and the production capabilities to deliver medical care innovations as safely and effectively and in as patient-centric a way as we need.

Consider what it costs an organization like ours to deal with the patchwork quilt of local, state, and national health care regulations that have absolutely no central theme to them at all. We have done some very preliminary estimates in our organization, and we think that we spend somewhere between 5 and 7.5 percent of our total revenue stream on meeting regulatory requirements. That is the regulatory burden that we have to pay. It is close to a billion dollars.

On the reimbursement side, the fee-for-service system is designed to reward individual acts by individual clinicians. If we think about the need to create integrated delivery capabilities, the reimbursement system we currently have does not support that very effectively. The *Crossing the Quality Chasm* report called for experimentation in a variety of reimbursement approaches to find those that would stimulate the creation of integrated delivery capabilities. It may be prepayment or capitation. There may be other tools as well, but the fact remains that the classic form of fee-for-service system is a barrier to the development of collaborative medicine.

LACK OF INVESTMENT IN INFORMATION TECHNOLOGY

The final major issue that we identified in the IOM report is the fact that IT is not being deployed into the delivery system in the way that one would expect for such an information-rich industry. We estimate that between one to two percent of total revenues in healthcare is now invested in IT infrastructure. We see much higher levels being invested on the health insurance side, but on the delivery system side it is still much lower than other industries or the medical technologies industry. I know the share of revenues of Agilent that is spent on the IT infrastructure is far higher than

what is spent in health care. Yet, health care is arguably one of the most information-rich decision-complex production systems on the planet. We are not making the required levels of investment in IT. Finding capital, either by aggregating organizations to generate the capital or creating other ways to build that capital, is a major issue. We cannot do the kind of innovation in health care delivery that matches the complexity of the science. If you are a physician trying to keep up with 10,000 randomized clinical trials in a year, how can you practice evidence-based medicine without an information technology decision support system? It simply is beyond the capacity of individuals to keep up. The progressive narrowing of the practice of medicine into deeper and deeper specialties may be a reaction to that, but even narrow specialists find it very difficult to keep current with the evidence.

THE OPPORTUNITIES FOR INNOVATION

So where are the opportunities for innovation? In my view the areas I identified as problems are the focal points for the innovations that we need to see on the delivery side.

Improving the Way Patients Interconnect with the Delivery System

The first priority for intervention is to improve the ways in which patients can connect with the medical care delivery system. We are talking about monitoring, diagnosis, and treatment technologies that enable the patient to self-manage or at least communicate on a regular ongoing basis with the health care system. It does not make sense to continue to invest heavily in the bricks and mortar of the classic delivery systems when there are other vehicles for taking care of patients in a far more responsive, patient-centric way. Both giving the tools to the patient and creating the bridges between the patient and the delivery system is one focus for innovation.

Let me be more specific. One of many promising innovations is the ability to test whether Coumadin is operating at therapeutic levels using a handheld testing device that is managed by the patient. This is just one of many examples. Blood sugar testing is another. There are many such devices that will substantially improve the connection between the patient and the system and put more capability in the hands of the patient. It also decreases our dependence on brick and mortar solutions for the delivery system.

Improving the Production Process

The second major area for innovation is to take the tools of manufacturing and production in goods and services and translate them into language that applies in health care. I would argue that the production of medical care today is the most complex production challenge that exists on the planet. Think about what is involved in running a hospital. There are about 250 beds, a wide array of diagnoses, a multitude of judgments being made by the team of professionals who interact with patients, plus all the support production that makes this happen hour after hour, 24 hours a day, seven days a week. It is an extraordinarily complex production challenge.

Today, we do not use the language of production in medicine, and we do not bring many of the tools of production design and monitoring to the task of taking care of patients, whether in the hospital or in the outpatient setting. Bringing the tools of production management and control to health care, translating them to health care, is an important innovation. This will require further changes in training, in team formation, and in communications.

So the second focus for innovation is at the micro level of production, taking care of diabetic patients, taking care of patients with cancer. We have a great deal to learn about how to put together those production systems. In introducing new systems approaches, we have to figure out ways to maintain the relationship between the caregiver and the patient, because this is where a great deal of the communication takes place, a great deal of the trust is created, and a great deal of the caring occurs. This is another substantial innovation challenge.

Moving from the current way in which most medical care is organized to the required level of sophistication is a long road, but we have to travel it. Given what is coming along in medical science and technology, how much more complexity that will be introduced into the caring for patients, and how much greater production design challenge that is going to create, we have to start soon.

Creating Larger Health Care Delivery Units

The third area of innovation involves organizational design or scaling. It has proven extremely difficult to figure out how to create sufficient scale on the delivery system side so that you can get the capital needed and the systems and the training capabilities and the other things that larger organizations can provide, applied to the delivery of care. We have been able to do it in certain health care settings for example, hospitals or nursing homes or laboratories or pharmacies. It has proven extremely difficult, however,

to create any kind of organizational scale for building integrated delivery capabilities. Kaiser Permanente has pulled back from 20-year experiments attempting to do that in four parts of the country. Efforts to expand by integrated delivery systems have proven almost impossible. Certainly very long periods of time are required before you can get it to succeed. Until we experiment with a variety of organizational forms, we are going to have a great deal of difficulty getting to any kind of scale that enables the creation of the infrastructure required. We have small islands of excellence around the country. But putting them together so that you begin the transformation of the entire system is going to be difficult. In the Institute of Medicine report we discussed self-organizing systems, drawing on the experiences of the military and some of the new theories about organizational design. But their application in health care is still in the very early stages.

Public Policy Initiatives

Lastly, opportunities exist at the national policy level to intervene in regulation, reimbursement, and, possibly, the financing of the information technology infrastructure in medicine.

It may be that the financing of the information technology infrastructure exceeds the capacity of the private marketplace, given the current organization of health care. Perhaps the state of medicine requires us to create the medical equivalent of the Superfund for environmental cleanup, focused on building the IT infrastructure for the delivery system. This involves more than the electronic medical record, which is simply a way of capturing and moving information to support decision making. A robust infrastructure would incorporate analytic tools that would enable study of the epidemiology of disease. Without this infrastructure it is going to be hard for us to test whether or not these micro production units are working well and whether we are getting anywhere with the larger organizational entities that are required to help get to some sort of scale.

Let me close by reiterating that the message of the Institute of Medicine's report, *Crossing the Quality Chasm*, is that the mismatch between the pace and scope of medical science and technological innovation and delivery system innovation has created a chasm. It is aggravated by the shifting demographics of the country and the shifting disease burden of the country to an increasingly chronic disease burden. The complexity that both bring to the task of taking care of patients has not been matched by an equivalent sophistication on the delivery system side. In response to these changes, we have created complexity on the delivery system side. But we have not turned that complexity into a delivery capability that matches the sophistication of what we are trying to do for patients.

DISCUSSION

Chuck Buck, General Electric (ret.): Clay Christiansen in his work on disruptive innovations talks about major changes in major industries often coming from stealth movements way down below the radar of the big companies like Kaiser Permanente. These movements then grow and they learn and they take on more and more over time.

Where will pockets of innovation start that will connect with the consumer and provide the systems approach that you talked about? I am wondering if it is not the groups of ten that you say are too small. Maybe those are the places to start to grow this. So how do you see this working through the marketplace?

David Lawrence: What I observe as I talk to physicians outside of Kaiser Permanente is that the impetus for innovation is largely coming from an interesting group of physicians, the cohort of physicians in their mid-thirties to mid-forties who have always driven innovation in medical care delivery. There is some very exciting innovation going on around the country that gives some hope that the transformation may occur from these isolated, fragmented groups of less than ten and may turn into something that looks like a virtual production capability.

At the moment, most of these groups are dealing with simple problems such as how they communicate more effectively among themselves. They have not yet gotten to the issue of how to create multidisciplinary teams to take care of chronic illness, for example, or how to deal with the production system underneath them so that it operates more efficiently. But they are at least a start.

To employers or purchasers I say, “Do not be captive of the mainstream delivery system.” There are solutions lurking out there that ought to be purchased or supported, for example, chronic disease management capabilities that may or may not be associated with a particular fixed geographic delivery system. Looking for these kinds of innovations, just as you do in purchasing everything you buy, is important.

Mary Jo Deering, Department of Health and Human Services: You have alluded to the disparity between the rate of growth of medical innovation and the pace of change in the industry, and you allude to this disparity as a chasm. Frankly, it sounds like the chasm is getting deeper and wider, and that is likely to become worse in the future. In terms of priorities for federal spending in the near to medium term, does that not suggest more investments should be focused on the system itself and on developing that infrastructure to absorb innovations?

David Lawrence: The simple answer is yes. I have despaired watching the congressional debate on the Patient’s Bill of Rights, saying, “Congratulations, you have just solved a non-problem. I hope you all get re-elected.”

An extraordinary amount of time, energy, and political clout is being spent on that question. It is probably a problem that needs to be solved, but it has nothing to do with the core issues.

Investments in the medical care delivery system are really where we have to go, and I think the federal government has a role to play in this, either as a purchaser or as an investor. As I said earlier, the need to develop the IT infrastructure may be a case of where government can have an impact. I would also like to see the federal government take the lead in dealing with the regulatory morass that we are facing in health care. I would also like to see the federal government experiment with different reimbursement approaches to see whether or not we can create integrated approaches for delivering care at the micro level. Triggering this transformation has to start at the micro level. At some point, we will get enough things aggregating that we can call them systems. But we are years away from even creating the right templates at the local level. I would like to see the federal government make some initiatives here. To paraphrase an ex-President's election mantra, "It is the delivery system, stupid."

Jean-Paul Gagnon, Aventis Pharmaceutical: In your IOM discussions did you talk about an electronic customer relationship management (eCRM) approach? One policy approach might be to have the government fund the Agency for Healthcare Research and Quality to support the development of eCRM. eCRM is consumer relationship management. It is an important movement now within many corporations to tie everything together, so that when the patient calls, whomever answers the phone has access immediately to how many times that patient has been in contact, who has been contacted, and what was discussed. The customer does not respond, "I've called this place 10 times, and now I've got to tell my whole story all over again."

David Lawrence: To do what you are talking about requires a communications infrastructure. It is very hard to collate information, when no one is linked to anyone else on the delivery side, which is the situation today. The impetus behind the clinical information system that we at Kaiser are investing about a billion and a half dollars in over the next 3 or 4 years is to do precisely that. But remember, the core problem is achieving any kind of scale that would aggregate enough of those contact points. The big problem for many patients is that they go from one health care silo to another. The only common thread is the patient and the patient's family. There is no system, there is no communications capability. There is not even consistent science that is being applied from place to place. To accomplish eCRM would require at least the identification of the types of organizational forms that would begin to pull together this highly fractionated system.

Kevin Finneran, Issues in Science and Technology, NRC: You mentioned the use of consumer-oriented home devices that people might use to

improve the control and management of their own health care. How can the use of these devices be facilitated through public policy initiatives, whether through reimbursement policies, regulations, or standards for the equipment? What stands in the way of greater use of consumer-oriented home devices?

David Lawrence: My biggest fear is not that they will not be used, but that they will be used out of coordination with the rest of the delivery system. I am more worried about the bridging systems than the innovations that will likely be very attractive to consumers. One of the fastest-growing areas of medical expenditure is for self-managed diagnostic and monitoring devices.

The key question is, how do you link these devices back into the delivery system, so that the patient's information is available and used? Agilent and other organizations have spent some time investigating what share of laboratory information on patients that actually gets into the patient's medical record of the health care institution. Only about 20 percent of all the information that is generated about the patient's status actually gets into the medical record and is usable by the medical care delivery system.

The barriers to the bridging process are my biggest concern. Obviously, lack of capital to build the bridging telecommunications systems is another concern. We are spending a substantial share of \$1.5 billion to build the communications links between the patients and our health care delivery system. Not many organizations have the capital available to do that.

There is one more issue that is a slight digression from what you are saying. One of the potential areas for technological breakthrough is not really in medical care per se, but are in quality of life enhancing capabilities. Let me give you two examples. If you had a stroke and you no longer can speak, you still think. You may be able to communicate by computer. Think of the person who is born with cerebral palsy, unable to speak, wonderful mind, great ideas, and unable to communicate those ideas except by computer with a pencil. How many people who are not in the work force can afford those technologies? Or think about the disabled person who wants to have access to a robotic wheelchair? It is now in the last stages of clinical trials through FDA. How do we pay for those? I do not know that the medical care system or medical insurance can pay for them, but we surely need a financing system for those kinds of technologies that are supplemental to what medical care would be delivering. That is another barrier.

David Gilman: You have very cheerfully presented a devastating landscape. It is hard to know where to begin. I think that one of our biggest problems, is knowing where we can make a significant difference without ripping up the whole thing and starting over again. What we need is a hit

list, where it might make the most difference to engage with the agencies and the Congress.

The things that you say should be done must be going on at Kaiser Permanente. Could you give us a couple of examples about teamwork at Kaiser Permanente? In connection with this notion of everything being fragmented, especially in the reimbursement area, we should try capitation models. You have a large-scale capitation model that we should know more about.

David Lawrence: Let me take your points in reverse order. Ed Wagner and Don Berwick are doing some very interesting work, trying to bring together the experiences of integrated delivery for specific diseases, primarily chronic illnesses, documenting the impact that the integrated delivery capability has on the outcomes and also the cost. There appears to be great promise in what they are doing. We see the same thing in Kaiser Permanente. Don Berwick has said in some of his comments to our people, “Whenever I want to find a best practice, the first place I go is Kaiser Permanente. I usually can find it there.” Unfortunately, it is just a best practice. The hardest thing in Kaiser Permanente, as it is in the rest of the country, is to move that science to standard practice. You do not tell doctors you need this; you do not tell professionals to do that.

I am very excited about where organizations like ours are moving around the issues of integrating at the micro level, and creating team-based approaches for care. We have a wide array of examples now, and are moving in that direction through something we call the Care Management Institute. This institute identifies not only the scientific base of how we should practice from a clinical guidelines point of view, but also what is the best evidence-supported way of organizing the delivery of care to achieve those outcomes. Then finally, the clinical information system, where implemented, has shown dramatic impacts on the ability of the infrastructure to organize in the way you have described.

So we have a number of examples. We still have a long way to go, like most health care organizations do. But I really believe that organizations like ours are about 10 to 20 years further up the learning curve than the rest of the health care system in terms of putting together these kinds of systems.

Turning to your question about what should be on the hit list. I think it is possible to put together more than one list. There is a public policy list addressing regulation at the macro level. That list should be broadened to include reimbursement, IT investment, and perhaps work force training and work force redeployment. The latter is a major impediment to making change in the health care system.

I would go back downstream to the patient and develop the health care connection hit list. What are the sorts of things that need to be done that could foster the development of really sophisticated and appropriate sys-

tems that link the patient most effectively to the medical care delivery system?

Then I would also develop a hit list around how one works at the micro level. The major investments that need to be made here, include, first, the training of physicians, and, second, translating the language and tools of organizational design for production and manufacturing industries into medical care. We simply do not have the language to talk about it in a way that works for us as professional caregivers.

Susan Foote, University of Minnesota: It occurred to me as I was listening that we have got a policy chasm as well as an organizational and delivery system chasm. I will talk a little bit about it later, but all this fragmentation and complexity that you talk about from the delivery side is reflected in the political side. There are institutional changes that have occurred internally in Congress, and entrepreneurial politics that have gotten in the way of big wise solutions.

But I think the provider side and the delivery system side has to take some responsibility for the condition of the public policy interventions. The Patient's Bill of Rights did not emerge from the minds of the members of Congress. It was requested by a fragmented group of individual providers and organizations who demanded it and then fought about it. There is an expectation that the political process can come in and think big. But all the representatives of the medical delivery system are in there, the nurse anesthetists versus the anesthesiologists fighting on payment.

The big picture will not come from the Congress *sui generis*, and it does not seem to be coming from any leadership on the private sector side. How are we going to break that syndrome to get to the solutions that you have identified?

David Lawrence: A wonderful question. One of the issues that we have been wrestling with is the analogies that can we draw from other industries, where fractured, fragmented, entrepreneurial activity somehow coalesced into a set of standards and approaches that then was reflected in a rational national policy. There are some analogues in the telecommunications industry. There may be some in other sectors as well. We need to look at that to see whether or not there are some lessons to be drawn about how to answer your question.

What is happening in Congress is a reflection of the fragmentation in the delivery system and the financing system. The financing system, the insurance side, actually is far better organized than the delivery system side is. The delivery system is fragmented by professional interest group (nurses, doctors, hospital administrators, and so on) and entrepreneurial activities (not-for-profit, for-profit).

I do not yet know where the opportunities lie for a few of the major

players on the delivery side to aggregate and create a political pressure point that would then encourage Congress to respond. Congress is nothing more than a reflection of the constituents. It is not going to come up with the big ideas on its own. We have watched that rise and fall once, and I do not think that is going to come again.

Stephen Merrill, NRC: When one thinks of federal investments in IT infrastructure, one thinks of one fantastically successful recent jumpstart, namely the Internet and several highly troubled internal systems like those of the Social Security Administration, Internal Revenue Service, and the Federal Aviation Administration. Do you have any model for how the federal government could invest in IT in health care successfully?

David Lawrence: Singapore may be showing us a way through the creation of an investment pool for IT experiments. Where does the capital come from to invest in the experiments and the tests and the kind of innovations that we spoke of earlier? It is not coming from Wall Street. It is not coming from private venture capital on the delivery system side. It is not coming from the health care systems themselves, because there is very little margin there.

So in my judgment the model is an investment bank model, which is not solution driven but experiment and innovation driven. If we could create that kind of a fund, I think we would then see a number of major experiments, not the kind of micro experiments that are going on now but major experiments. Out of that we would begin to define a way forward.